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**In the Supreme Court of the United States**

OCTOBER TERM, 1978

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UNITED STATES OF AMERICA, ET AL., PETITIONERS

*v.*

GLEN L. RUTHERFORD, ET AL.

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**PETITION FOR A WRIT OF CERTIORARI TO THE  
UNITED STATES COURT OF APPEALS  
FOR THE TENTH CIRCUIT**

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The Solicitor General, on behalf of the United States, *et al.*, petitions for a writ of certiorari to review the judgment of the United States Court of Appeals for the Tenth Circuit.

**OPINIONS BELOW**

The opinion of the court of appeals (App. A, *infra*, 1a-7a) is not yet reported. The opinion of the district court (App. D, *infra*, 11a-44a) is reported at 438 F. Supp. 1287. The decision of the Commissioner of the Food and Drug Administration (App. E, *infra*, 45a-274a) is reported at 42 Fed. Reg. 39768.

### JURISDICTION

The judgment of the court of appeals (App. B, *infra*, 8a-9a) was entered on July 10, 1978. On August 4, 1978, the court of appeals summarily denied a Motion for Clarification or in the alternative Petition for Re-Hearing filed by respondents on July 27, 1978 (App. C, *infra*, 10a). The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

### QUESTION PRESENTED

Whether the safety and effectiveness requirements of the Federal Food, Drug, and Cosmetic Act apply to drugs intended for use by the terminally ill.

### STATUTES INVOLVED

Section 201(p) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321(p), provides in part:

The term "new drug" means—(1) Any drug \* \* \* the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this Act it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use \* \* \*

Section 107(c)(4) of the Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 789 ("1962 grandfather clause"), provides:

In the case of any drug which, on the day immediately preceding the enactment date [October 10, 1962], (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force [21 U.S.C. 231(p)], and (C) was not covered by an effective [new drug] application under section 505 of that Act [21 U.S.C. 355], the amendments to section 201 (p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

Section 505 of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 355, provides in part:

(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug.

(b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use \* \* \*

\* \* \*

(d) If the Secretary finds \* \* \* that (1) the investigations \* \* \* required to be submitted to



the Secretary \* \* \* do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests \* \* \* do not show that such drug is safe for use under such conditions; \* \* \* (4) \* \* \* he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) \* \* \* there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. \* \* \* As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

\* \* \* \* \*

(i) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to

investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(1) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing  
\* \* \*

#### STATEMENT

The Federal Food, Drug, and Cosmetic Act of 1938, ch. 675, 52 Stat. 1040 *et seq.*, prohibited the introduction of any new drug into interstate commerce without the approval of the Secretary of Health, Education and Welfare.<sup>1</sup> The Act provided procedures for filing applications for such approval, and directed the Secretary to deny approval if he did not find, on the basis of adequate scientific evidence, that the drug was safe for its intended use. Section 355(d), 52 Stat. 1052. The Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780, substantially amended

<sup>1</sup> The Secretary has delegated this authority to the Commissioner of the Food and Drug Administration (FDA). 21 C.F.R. 5.1(a). Under the 1938 Act, a "new drug" was one not generally recognized by qualified experts as safe for its intended use (Section 201(p), 52 Stat. 1041). The Act contained a "grandfather clause" excluding from the definition of "new drug" any drug that, before enactment of the 1938 Act, was subject to the Food and Drugs Act of 1906, ch. 3915, 34 Stat. 768, and that retained representations concerning the conditions of use identical to those it then had. This 1938 grandfather clause remains in the current Act. 21 U.S.C. 321(p)(1).

the 1938 Act. They redefined a new drug as one not generally recognized as effective as well as safe (Section 201(p)(1), 21 U.S.C. 321(p)(1)). And they directed the Secretary to deny approval of a new drug application unless he finds substantial evidence<sup>2</sup> that the drug is effective for its intended use, as well as safe. 21 U.S.C. 355(d). See *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 612-615 (1973).<sup>3</sup>

This action was instituted by cancer patients on March 12, 1975,<sup>4</sup> and seeks to prevent the government

<sup>2</sup> "Substantial evidence" is defined as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof." Section 505(d), 21 U.S.C. 355(d).

<sup>3</sup> The 1962 Amendments also contain a grandfather clause, excluding from the definition of "new drug" any drug that, on October 9, 1962 (the day immediately preceding the enactment of the 1962 Amendments): "(A) was commercially used or sold in the United States, (B) was not a new drug [under the 1938 Act] \* \* \* and (C) was not covered by an effective [new drug application]." Section 107(c)(4), 76 Stat. 789.

<sup>4</sup> The action was originally instituted by Juanita Stowe, a cancer patient, and her husband Jimmie Stowe. After Mrs. Stowe's death, an amended complaint was filed by two other patients, Glen L. Rutherford and Phyllis S. Schneider, and Mrs. Schneider's husband, on behalf of a class composed of cancer patients and their spouses who are responsible for the costs of treatment. Mrs. Schneider subsequently died. By order entered April 8, 1977, the district court certified this case as a class action on behalf of a class composed of ter-

from interfering with the interstate sale or distribution of a drug called Laetrile. In an order entered August 14, 1975, and amended October 10, 1975, the district court enjoined the government from preventing the purchase and subsequent interstate movement of a limited quantity of Laetrile for Glen L. Rutherford, one of the plaintiffs. *Rutherford v. United States*, 399 F. Supp. 1208, 1215 (W.D. Okla. 1975).<sup>5</sup> On appeal, the Tenth Circuit did not disturb the injunction, but instructed the district court to remand the case to the Commissioner of Food and Drugs for the development of an administrative record addressing the questions whether Laetrile is a "new drug" within the meaning of Section 201(p) and, if so, whether it is exempt from the premarketing approval requirements of the Act by virtue of the Act's 1938 or 1962 grandfather clauses. *Rutherford v. United States*, 542 F.2d 1137 (10th Cir. 1976).<sup>6</sup>

On remand, the Commissioner concluded after an administrative proceeding that Laetrile is a "drug" as defined in the Act, because it is being sold for the cure or prevention of disease, and a "new drug" within the meaning of Section 201(p) of the Act, 21 U.S.C. 321(p). App. E, *infra*. He found that Laetrile does not satisfy the premarketing approval re-

minally ill cancer patients, *Rutherford v. United States*, 429 F. Supp. 506, 509 (W.D. Okla. 1977). The propriety of that order was not appealed by the government.

<sup>5</sup> The district court subsequently entered similar orders on behalf of other plaintiffs.

<sup>6</sup> See notes 1 and 3, *supra*.

quirements for new drugs in Section 505 of the Act, 21 U.S.C. 355, because it does not meet the statutory safety and effectiveness requirements. The Commissioner found that there is "an absence of scientifically sound data upon which experts \* \* \* could base an opinion that Laetrile is safe for use in man" (*id.* at 157a), and that "[t]here are no clinical investigations of Laetrile's effectiveness, published or otherwise, which are even arguably adequate and well-controlled." *Id.* at 93a-94a.

The Commissioner further found that Laetrile does not meet the statutory criteria of either the 1938 or the 1962 grandfather clause: The drug presently termed "Laetrile" was not shown to be the same drug used during the applicable prior period; the prior labeling and representations concerning use are not identical to the representations associated with the presently marketed drug; Laetrile was not commercially used or sold on the grandfather date; and experts did not generally recognize it as safe on that date. *Id.* at 163a-211a.

On review of the Commissioner's decision, the district court upheld his determination that Laetrile is a drug, and further held that "the evidence of record does not render the Commissioner's conclusion that Laetrile is not 'generally recognized as safe and effective' arbitrary and capricious." App. D, *infra*, 22a. The court concluded, however, that the drug is exempt from the Act's premarketing approval requirements by virtue of the 1962 grandfather clause. In reaching this conclusion, the court set aside each

of the Commissioner's factual findings on the issue. App. D, *infra*, 26a-34a. The court further concluded that "[b]y denying the right to use a nontoxic substance in connection with one's own personal health-care, FDA has offended the constitutional right of privacy." *Id.* at 41a (footnote omitted).<sup>7</sup>

The court of appeals, without addressing either the statutory or the constitutional ground on which the district court relied, concluded that the Commissioner had misinterpreted the safety and effectiveness requirements of the Act as applied to "persons who are \* \* \* fatally stricken with a disease for which there is no known cure." App. A, *infra*, 6a. In the court's view, "[c]learly the terms have no meaning under these circumstances, and certainly not the abstract meaning sought to be applied by the Commission[er]." *Ibid.* The court therefore held that "the 'safety' and 'effectiveness' requirements of the statute as now written have no application to terminally ill cancer patients who desire to take [Laetrile] intravenously." *Id.* at 7a. The court emphasized that its decision applied only to the intravenous use of Laetrile by terminally ill cancer patients, a group whose members, it concluded, could be identified without difficulty by the certification of a licensed medical

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<sup>7</sup> In reaching this conclusion the court expressly rejected (App. D, *infra*, 29a n. 18 and 31a-34a nn. 23, 24) the Commissioner's factual finding (App. E, *infra*, 157a, 162a, 273a-274a) that Laetrile has a known toxicity that has not been fully investigated.



practitioner. *Id.* at 5a-6a.<sup>8</sup> The Food and Drug Administration was directed to "promulgate regulations within the above limitations and as if the drug was found by the Commission[er] to be 'safe' and 'effective' for the limited group of persons here considered." *Id.* at 7a.

#### REASONS FOR GRANTING THE PETITION

The court of appeals' construction of the Federal Food, Drug, and Cosmetic Act is contrary to the plain meaning of the statute, its legislative history, and its uniform interpretation by the agency responsible for its enforcement. The court's decision seriously limits the Commissioner's power to protect the public from unsafe and ineffective drugs. Although the present ruling is limited to the intravenous use of Laetrile by terminally ill cancer patients, the court's analysis of the Act would prevent the Commissioner from concluding that any drug intended for use by the terminally ill has not been shown to be safe and effective. The decision thus would make it difficult if not impossible for the Commissioner to discharge his statutory responsibility to keep unproven drugs out of the marketplace.<sup>9</sup>

<sup>8</sup> Plaintiffs' motion for clarification or rehearing, which requested the court to authorize the class members to take Laetrile orally, was denied without comment. App. C, *infra*, 10a.

<sup>9</sup> The decision is also inconsistent with *Rutherford v. American Medical Ass'n*, 379 F. 2d 641 (7th Cir. 1967), cert. denied, 389 U.S. 1043 (1968). In that case, a doctor and "hopeless"

1. The Federal Food, Drug, and Cosmetic Act contains no exemption from its premarketing clearance requirements for drugs intended for use by the terminally ill. The statute provides that no new drug may be introduced into interstate commerce unless the Commissioner has approved a new drug application. Section 505(a), 21 U.S.C. 355(a). That approval requires (1) the submission of reports that include "adequate tests by all methods reasonably applicable to show [that] such drug is safe for use," and (2) "evidence consisting of adequate and well-controlled investigations" showing that "the drug will have the effect it purports or is represented to have \* \* \*." 21 U.S.C. 355(d).<sup>10</sup> Nothing in the statute suggests

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cancer patients (379 F. 2d at 642) sought to enjoin FDA and others from interfering with the distribution of another drug allegedly effective in the treatment of cancer. The court held that "initial approval or exemption of a drug is within the primary jurisdiction of the FDA." *Id.* at 643. In the absence of any good faith application to the agency for such approval or exemption, the court lacked jurisdiction to review the refusal to permit the marketing of the drug. The opinion notes that Section 355 of the Act establishes a procedure for submitting adequate scientific information about a new drug to the FDA to "permit an intelligent assessment of its safety and efficacy" (*ibid.*). The court thus indicated that such an assessment was necessary for drugs designed for use by cancer patients, even "hopeless" ones; there is no suggestion that the court believed the standards of safety and effectiveness were less stringent for such drugs, let alone inapplicable.

<sup>10</sup> The only drugs exempted from these premarketing clearance requirements are those that are not "new." See notes 1 and 3, *supra*; *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 629-630 (1973).



that these requirements are not fully applicable to drugs intended for use by the terminally ill.<sup>11</sup> Nor is it appropriate to read such an exemption into the Act, as the court of appeals did, whether for terminal cancer patients or for persons terminally ill from any other affliction.

The court was incorrect in its view that safety and effectiveness have "no meaning" as applied to drugs to be used by such persons (App. A, *infra*, 6a).<sup>12</sup> It is entirely reasonable to give those terms the same meaning in this context that they have when applied to any other drugs. Neither term means, as the court evidently assumed, that the drug will cure the affliction for which it is taken. Instead, as the statute makes clear, a drug is "effective" if substantial evidence<sup>13</sup> indicates that it "will have the effect it purports or is represented to have under

<sup>11</sup> In discussing the court of appeals' holding we assume, like the court, that the "terminally ill" are an objectively identifiable group (App. A, *infra*, 6a). But the term is a prediction concerning the future course of a disease, rather than an objective description of an ailment, and is thus inherently speculative. See page 16, *infra*.

<sup>12</sup> The court was not entirely consistent in this view, since it evidently concluded that there are some appropriate safety limitations even for Laetrile. Thus, it required that the drug be administered by a physician and it limited its holding to intravenous administration, denying a petition requesting that it amend its order to allow oral dosages. This denial was unexplained, but presumably reflected a judgment by the court of appeals on the safety issue. See App. C, *infra*, 10a; App. D, *infra*, 29a n. 18; App. E, *infra*, 75a, 88a, 157a-162a, 254a-257a, 273a-274a.

<sup>13</sup> See note 2, *supra*.

the conditions of use prescribed, recommended, or suggested in [its] proposed labeling." 21 U.S.C. 355 (d); see S. Rep. No. 1744, 87th Cong., 2d Sess. 16 (1962). And a drug is "safe" if its benefits—either therapeutic or palliative—outweigh any adverse effects of its use; that is, if it will not gratuitously harm the person taking it.<sup>14</sup>

The terminally ill, whether victims of cancer or any other disease, have as much interest as the general public in protection from drugs that are not both safe and effective. Indeed, as the Commissioner noted (App. E, *infra*, 224a-230a), the vulnerable psychological state of cancer patients may make them particularly susceptible to unfounded claims and thus create a special need for protection from ineffective drugs.

Nothing in the legislative history supports the court of appeals' assumption that Congress could not have intended to impose safety and effectiveness requirements on drugs to be used by terminally ill cancer patients. Instead, remarks during congressional debate on the 1962 Amendments to the Act—which added the effectiveness requirement for new drugs,

<sup>14</sup> That harm may consist of hastening the person's demise or of causing less serious physical injury. Even in the absence of direct physical injury, the drug may cause harm by imposing an unwarranted financial burden on the patient and his family or by leading him to forego more effective treatment. See page 15, *infra*. As Senator Kefauver stated when introducing the bill that became the 1962 Amendments, "an otherwise completely safe drug can be dangerous to the patient if it does not have the therapeutic effect in use which it is represented to have." 107 Cong. Rec. 5640 (1961).

see *Weinberger v. Hynson, Westcott & Dunning, supra*—reflect an understanding that the Act would apply to experimental drugs used to treat “cancer in its last stages.” 108 Cong. Rec. 17399 (1962) (remarks of Sen. Kefauver, chairman of the committee reporting the bill).<sup>15</sup>

Thus, neither the statute nor its legislative history is ambiguous concerning the applicability of the Act to drugs intended for use by the terminally ill. But even if there were some ambiguity, the court’s narrow interpretation of the statutory requirements would be inconsistent with this Court’s repeated statement of the need to give a broad interpretation to the Act in order to facilitate the congressional policy of protecting the public health. *E.g., United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969); *United States v. Dotterweich*, 320 U.S. 277, 280 (1943).

2. The consistent administrative practice under the Act is also contrary to the conclusion of the court

<sup>15</sup> Senator Eastland, another proponent of the bill, also assumed that drugs administered for “fatal diseases, such as cancer,” would be subject to the Act’s requirements, noting that approval of such drugs would be appropriate even though they might only prolong life or alleviate suffering. 108 Cong. Rec. 17401 (1962).

References to cancer were also made during consideration of the 1938 Act. See, *e.g.*, 79 Cong. Rec. 5023 (1935) (remarks of Sen. Copeland, sponsor of the Act); 83 Cong. Rec. 7786-7787, 7789 (1938) (remarks of Reps. Phillips and Lea). See also Dunn, *Federal Food, Drug and Cosmetic Act* 42, 58, 77, 200, 639, 726, 952-956 (1938) (collecting the legislative history).

of appeals. The Food and Drug Administration has consistently interpreted the Act to require that drugs intended for the treatment of terminally ill persons satisfy the same statutory criteria of safety and effectiveness that are applied to all other new drugs.<sup>16</sup> That interpretation, which was ratified by Congress when it amended the Act in 1962,<sup>17</sup> is entitled to substantial judicial deference. See *e.g., United States v. An Article of Drug . . . Bacto-Unidisk, supra*, 394 U.S. at 791-792; *Red Lion Broadcasting Co. v. FCC*, 395 U.S. 367, 380-381 (1969); *Investment Company Institute v. Camp*, 401 U.S. 617, 626-627 (1971); *Udall v. Tallman*, 380 U.S. 1, 16 (1965).

Such deference is particularly fitting here, in light of the Commissioner’s finding (App. E, *infra*, 270a) that a decision such as that ultimately reached by the court of appeals

\* \* \* would lead to needless deaths and suffering among (1) patients characterized as “terminal”

<sup>16</sup> For example, there are approximately forty drugs presently approved for use in the treatment of cancer, without regard for whether it is terminal.

The Director of the National Cancer Institute recently announced that the Institute wishes to conduct controlled clinical tests of Laetrile use by several hundred advanced cancer patients. The Commissioner of FDA has indicated that he will promptly review any application received from the Institute for approval of such tests.

<sup>17</sup> In enacting the 1962 Amendments, which adopted the effectiveness requirement for all new drugs, Congress approved the FDA’s longstanding policy of requiring a demonstration of effectiveness for drugs used in the treatment of life-threatening diseases. S. Rep. No. 1744, 87th Cong., 2d Sess. 15 (1962); H.R. Rep. No. 2464, 87th Cong., 2d Sess. 3 (1962).

who could actually be helped by legitimate therapy and (2) patients clearly susceptible to the benefits of legitimate therapy who would be misled as to Laetrile's utility by the limited approval program or who would be able to obtain the drug through the inevitable leakage in any system set up to administer such a program.

This finding was supported by expert medical and technical testimony indicating that there is no way of distinguishing accurately between "terminal" cancer patients and those who will respond to conventional cancer treatment (*id.* at 267a-268a; see *id.* at 98a), and that even if such a distinction could be reliably made, it would be virtually impossible as a practical matter to restrict the use of Laetrile to the terminally ill (*id.* at 269a-270a).

The Commissioner, exercising his statutory responsibility for evaluating medical and technical testimony in this area, adopted this testimony (*id.* at 269a-270a). The court of appeals nevertheless concluded, without citation of authority, that:

It would not seem difficult to define the group [of terminally ill cancer patients]. A licensed medical practitioner can express an opinion as to whether, under the present state of the art, a particular person is terminally ill with cancer, and \* \* \* so certify.

We are well aware of and have considered the arguments that some patients will be victimized by unscrupulous persons who will seek to profit by offering Laetrile as a "cure." This is however not a legal matter, but an administrative or regulatory problem for the FDA. [App. A, *infra*, 6a-7a.]

This Court recently condemned a similar judicial interference with the proper exercise of authority entrusted to an agency by Congress. *Vermont Yankee Nuclear Power Corp. v. Natural Resources Defense Council, Inc.*, No. 76-419 (April 3, 1978), slip op. 35-36. So here, in what is likewise a distinctly technical area, the court of appeals should not have substituted its own judgment concerning the desirability of a special standard—that is, no standard at all—for drugs for the "terminally ill" in place of the determination of Congress and the Commissioner that such an exception from the statutory requirements is neither appropriate nor feasible.<sup>18</sup>

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Since the court of appeals has misconstrued the Act in a way that significantly endangers the public health, we submit that plenary review by this Court

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<sup>18</sup> The court directed the FDA to "promulgate regulations \* \* \* as if the drug was found by the Commission[er] to be 'safe' and 'effective' for the limited group of persons here considered" (App. A, *infra*, 7a). It is difficult to see how FDA could comply. In the absence of adequate data, there is no basis on which to label Laetrile in the manner required by Section 502, 21 U.S.C. 352. Directions for drug use, including indications, contraindications, dosages and routes of administration, warnings, side effects, and necessary collateral measures are premised on a body of data derived from extensive testing. As the Commissioner found, such data do not exist for Laetrile (App. E, *infra*, 93a-211a, 270a-272a). Neither court below disagreed with this conclusion. Without such testing data, the drug cannot be labeled for any use. Any suggestion in labeling that the drug may be safely or effectively used would misbrand the drug in violation of Sections 502(a) and 505(d)(6), 21 U.S.C. 352(a) and 355(d)(6).



is warranted. In the course of that review, respondents can be expected to argue that the judgment of the court of appeals should be affirmed on the grounds adopted by the district court but not reached by the court of appeals. See *United States v. New York Telephone Co.*, 434 U.S. 159, 166 n.8 (1977). We accordingly would discuss those grounds in our brief on the merits. We would argue that neither the 1962 grandfather clause nor the Constitutional right to privacy precludes the Commissioner's refusal to permit the interstate transportation of Laetrile. We have not discussed those issues in this petition because they do not affect the need for review of the court of appeals' decision and they were not dealt with in that decision. Without regard to those issues, the court of appeals' misinterpretation of the extent of the Commissioner's statutory authority to protect the terminally ill should be corrected by this Court.

## CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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OCTOBER 1978

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APPENDIX A

UNITED STATES COURT OF APPEALS  
TENTH CIRCUIT

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No. 77-2049

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[Filed Jul. 10, 1978]

GLEN L. RUTHERFORD, individually and on behalf of a  
class composed of terminally ill cancer patients,  
PLAINTIFFS, APPELLEES,

v.

UNITED STATES OF AMERICA, JOSEPH A. CALIFANO,  
SECRETARY OF HEALTH, EDUCATION AND WELFARE;  
DONALD KENNEDY, COMMISSIONER OF THE FOOD  
AND DRUG ADMINISTRATION, et al., DEFENDANTS,  
APPELLANTS

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APPEAL FROM THE UNITED STATES DISTRICT COURT  
FOR THE WESTERN DISTRICT OF OKLAHOMA

(D.C. # CIV-75-0218-B)

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Barry Grossman, Attorney, Department of Justice  
(John H. Shenefield, Assistant Attorney General,  
Catherine G. O'Sullivan, Attorney, Department of

Justice, Peter L. De La Cruz, Attorney, Department of Justice; of Counsel, Richard M. Cooper, Chief Counsel, Eugene M. Pfeifer, Associate Chief Counsel for Enforcement, and Arnold I. Friede, Assistant Chief Counsel for Enforcement, Food and Drug Division, Department of Health, Education and Welfare, with him on the Brief), for Appellants.

Kenneth Coe, of Looney, Nichols, Johnson & Hayes, Oklahoma City, Oklahoma, for Appellees.

Charles F. Wheatley, Jr., William T. Miller, Grace Powers Monaco, Robert A. O'Neil, of Wheatley & Miller, Washington, D.C., on the Brief for Amicus American Cancer Society.

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Before SETH, Chief Judge, BARRETT and McKAY, Circuit Judges.

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SETH, Chief Judge.

The Government appellants seek review of a district court holding which set aside a determination of the Commission of Food and Drugs that Laetrile, a controversial cancer drug, is a "new drug" within the meaning of the Federal Food, Drug, and Cosmetic Act ("the Act"), 21 U.S.C. § 301 *et seq.*, and thus excludable from interstate commerce due to the absence of an approved new drug application.

The central question here is whether the plaintiffs, *a class of terminally ill cancer patients*, should be

allowed to acquire Laetrile for their own use intravenously despite the Act's requirements that "safety" and "effectiveness" be established for the approval of a "new drug." We conclude as a matter of law that the "safety" and "effectiveness" terms used in the statute have no reasonable application to terminally ill cancer patients, and have no established meaning when considered in that context.

This case is before us for the second time. For a summary of the facts, *see* Rutherford v. United States, 542 F.2d 1137 (10th Cir.), and Rutherford v. United States, 438 F.Supp. 1287. In Rutherford v. United States, 542 F.2d 1137 (10th Cir.), we held that an adequate administrative record had not been developed by the Commissioner to justify classifying Laetrile as a new drug. We remanded and said:

"... To support its determination the FDA in the case at bar would have to present substantial evidence to support the proposition that Laetrile is not generally recognized among qualified experts as 'safe and effective,' and that Laetrile is not grandfathered by either of the exemptions discussed above."

We also upheld a preliminary injunction granted by the district court which prevented the FDA from interfering with a cancer patient's personal use of the drug.

On remand, the Commissioner compiled some 5,500 pages of written submissions and held two days of oral hearings before making a determination. This

was apparently a rule-making proceeding under section 701 of the Act, 21 U.S.C. § 371. The unsworn material compiled by the agency represents diverse views but does not appear to be the typical record which should be formulated to support an agency determination which is dealing with issues of scientific and medical expertise or in response to our remand. However, we fully realize difficulties in making a record when the proponents of a drug are a group of individuals and not the typical drug manufacturer who conducted extensive laboratory tests and assembled a mass of scientific data. The FDA was considering what may be regarded as a folk medicine with no established or organized proponents. This was difficult to do within the structure of the agency.

After consideration of the record on remand, the Commissioner announced that: (1) Laetrile is not generally recognized by qualified experts as a safe and effective cancer drug; and (2) Laetrile is not exempt from the premarket approval requirement for new drugs by virtue of the "grandfather" provisions of the Act. Distribution of Laetrile in interstate commerce, the Commissioner concluded, is thus illegal and subject to regulatory activity by the Food and Drug Administration.

The district court reviewed the administrative record and concluded that the decision of the Commissioner was "arbitrary and capricious" with regard to the 1962 grandfather exemption. The district

court also held that the provisions of the Act violated a cancer patient's constitutional right to privacy by denying him the right to use a nontoxic substance in connection with his own personal health care. A permanent injunction was issued by the district court.

While the FDA should make the initial determination as to "new drug" status, this decision is reviewable under 5 U.S.C. § 706(2). *Weinburger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609. In reviewing the FDA's determination the court should decide *inter alia*, "all relevant questions of law." 5 U.S.C. § 706. In *Rutherford* we remanded to the FDA for a determination on "safety" and "effectiveness," prerequisites which must be established for new drug approval. However, as these criteria are applied to terminally ill cancer patients, we noted some doubt in the application of the terms:

"The FDA argues that a drug offered for use in a life-threatening disease that is not 'effective' is thereby not 'safe' either. Thus even under the pre-1962 law Laetrile would have to satisfy effectiveness criteria. This argument may lose its force in the case of a terminally-ill patient or in the case of a patient suffering from a disease for which there are in fact no 'effective' remedies."

542 F.2d 1137, 1142, n. 5.

We are considering only cancer patients who are terminally ill and only their intravenous use of Laetrile. Thus in this context, what can be "generally



recognized" as "safe" and "effective" mean as to such persons who are so fatally stricken with a disease for which there is no known cure? What meaning can "effective" have in the absence of anything which may be used as a standard? Under this record Laetrile is as effective as anything else. What can "effective" mean if the person, by all prevailing standards, and under the position the Commission takes, is going to die of cancer regardless of what may be done. Thus there has been no standard here advanced by the Commission against which to measure the safeness or effectiveness of the drug as to the plaintiffs. Clearly the terms have no meaning under these circumstances, and certainly not the abstract meaning sought to be applied by the Commission. This was an erroneous application of the Act by the Commission. We do not say that *anything* is safe for the persons here concerned and *nothing* is effective, but it is apparent that no applicable or reasonable measure exists.

It would not seem difficult to define the group to which this determination of a legal issue applies. A licensed medical practitioner can express an opinion as to whether, under the present state of the art, a particular person is terminally ill with cancer, and to so certify.

We are well aware of and have considered the arguments that some patients will be victimized by unscrupulous persons who will seek to profit by offering Laetrile as a "cure." This is however not a legal

matter, but an administrative or regulatory problem for the FDA.

Therefore, we hold as a matter of law that the "safety" and "effectiveness" requirements of the statute as now written have no application to terminally ill cancer patients who desire to take the drug intravenously.

We do not reach the constitutional aspects which were applied by the district court. We conclude, however, that the permanent injunction granted by the district court should be continued but be limited only to permit procurement of intravenous injections administered by a licensed medical practitioner to persons who are certified by a licensed medical practitioner to be terminally ill of cancer in some form.

We are confident that the FDA with all due dispatch will promulgate regulations within the above limitations and as if the drug was found by the Commission to be "safe" and "effective" for the limited group of persons here considered.

The case is remanded for further proceedings consistent with this opinion.



## APPENDIX B

UNITED STATES COURT OF APPEALS  
FOR THE TENTH CIRCUIT

No. 77-2049

GLEN L. RUTHERFORD, individually and on behalf of  
a class composed of terminally ill cancer patients,  
PLAINTIFFS-APPELLEES,

*vs.*

UNITED STATES OF AMERICA, JOSEPH A. CALIFANO,  
SECRETARY OF HEALTH, EDUCATION AND WELFARE;  
DONALD KENNEDY, COMMISSIONER OF THE FOOD  
AND DRUG ADMINISTRATION, ET AL., DEFENDANTS-  
APPELLANTS.

Before Honorable Oliver Seth, Honorable James E.  
Barrett, and Honorable Monroe G. McKay, Circuit  
Judges.

This cause came on to be heard on the record on  
appeal from the United States District Court for the  
Western District of Oklahoma, and was argued by  
counsel.

Upon consideration whereof, it is ordered that the  
judgment of that court is affirmed in part and modi-  
fied in part. The cause is remanded to the United  
States District Court for the Western District of  
Oklahoma, with directions to modify its permanent  
injunction granted December 5, 1977, so as to limit  
it in its future application only to permit procure-

ment of Laetrile for intravenous injections adminis-  
tered by a licensed medical practitioner to persons  
who are certified by a licensed medical practitioner to  
be terminally ill of cancer in some form. Thereafter,  
the trial court shall remand the case to the Food and  
Drug Administration for further proceedings con-  
sistent with this opinion.

/s/ Howard K. Phillips  
HOWARD K. PHILLIPS  
Clerk

## APPENDIX C

*MAY TERM—August 4, 1978*

Before The Honorable Oliver Seth, Circuit Judge  
The Honorable James E. Barrett, Circuit Judge  
The Honorable Monroe G. McKay, Circuit Judge

No. 77-2049

GLEN L. RUTHERFORD, individually and on behalf of a  
class composed of terminally ill cancer patients,  
PLAINTIFFS-APPELLEES

*vs.*

UNITED STATES OF AMERICA, JOSEPH A. CALIFANO,  
Secretary of Health, Education and Welfare;  
DONALD KENNEDY, Commissioner of the Food and  
Drug Administration, et al., DEFENDANTS-APPEL-  
LANTS

AMERICAN CANCER SOCIETY, AMICUS CURIAE

(In support of Petitioners)

This matter comes on for consideration of the mo-  
tion for clarification, or in the alternative, petition for  
re-hearing filed by appellee Glen L. Rutherford on  
July 27, 1978.

Upon consideration whereof, it is ordered:

1. The petition for rehearing is denied.
2. The motion for clarification is denied.

/s/ Howard K. Phillips  
HOWARD K. PHILLIPS  
Clerk

## APPENDIX D

UNITED STATES DISTRICT COURT  
W. D. OKLAHOMA

No. CIV-75-0218-B

Dec. 5, 1977

GLEN L. RUTHERFORD, Individually and on behalf of  
a class composed of terminally ill cancer patients,  
PLAINTIFFS

*v.*

UNITED STATES OF AMERICA, JOSEPH A. CALIFANO,  
Secretary of Health, Education and Welfare;  
DONALD KENNEDY, Commissioner of the Food and  
Drug Administration, et al., DEFENDANTS

## OPINION

BOHANON, District Judge.

The plaintiffs seek judicial review of the Food and  
Drug Administration's (FDA's) determination that  
the substance commonly called Laetrile is a "new  
drug" within the meaning of the Federal Food, Drug,  
and Cosmetic Act, (the Act); (21 U.S.C. § 301 et  
seq.), and excludable from interstate commerce due  
to the absence of an approved new drug application  
on its behalf. (21 U.S.C. § 355).

On July 29, 1977, the Commissioner of Food and  
Drugs announced that: (1) Laetrile is not generally  
recognized by qualified experts as a safe and effective

cancer drug and (2) Laetrile is not exempt from the pre-market approval requirement for new drugs by virtue of the "grandfather" provisions of the Act. Distribution of Laetrile in interstate commerce, the Commissioner concluded, is thus illegal and subject to regulatory activity by the Food and Drug Administration. Commissioner's Decision (R 523 at 1).<sup>1</sup>

Plaintiffs challenge such administrative decision and urge that Laetrile is not a "drug," that in any event it is not a "new drug," and that FDA's enforcement procedures against the interstate transportation and use of the substance violate plaintiffs' constitutional rights.

## I

### STANDARD OF REVIEW

FDA possesses jurisdiction to initially determine whether a substance is a "new drug" within the Act's meaning, *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609, 627, 93 S.Ct. 2469, 37 L.Ed.2d 207 (1973), but such determination is reviewable by the district court under the Administrative Procedure Act, 5 U.S.C. § 701 et seq., *Weinberger, supra*. To be affirmed, the administrative decision must not be arbitrary, capricious or abusive of agency discretion.<sup>2</sup>

<sup>1</sup> In adopting the approach employed by FDA, submissions to the administrative record are designated by an R followed by the number assigned to them by the Hearing Clerk. References to the transcript of the oral argument are cited as Tr.

<sup>2</sup> 5 U.S.C. § 706 states in part: "To the extent necessary to decision and when presented, the reviewing court shall

*Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 416, 91 S.Ct. 814, 28 L.Ed.2d 136 (1971). The court in its review must consider whether the decision was based upon a consideration of the relevant factors and whether there has been a clear error of judgment.<sup>3</sup> *Citizens to Preserve Overton Park v. Volpe, supra*.

While the standard of review is narrow, and the court is not empowered to substitute its judgment for that of the agency, nonetheless, the reviewing court possesses a responsibility "to engage in a substantial inquiry," and "his inquiry into the facts is to be searching and careful. . . ." *Citizens to Preserve*

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decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall— . . . (2) hold unlawful and set aside agency action, findings, and conclusions found to be—(A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law . . . ." (emphasis supplied)

<sup>3</sup> The Tenth Circuit Court of Appeals has clearly established previously that Laetrile is not to be considered a "new drug" merely because the FDA has said so; the agency must proffer "substantial evidence" supportive of such determination. *Rutherford v. United States*, 542 F.2d 1137, 1143 (10th Cir. 1976). "Perhaps agency action which is not based upon substantial evidence is arbitrary and capricious." *American Petroleum Institute v. EPA*, 540 F.2d 1023, 1028 (10th Cir. 1976).

<sup>4</sup> A court may study the record, hopefully perceptively, even as to the evidence on technical and specialized matters, and penetrate to the underlying decisions of the agency, to satisfy itself that the agency has exercised a reasoned discretion and has not deviated from or ignored the ascertainable legislative



*Overton Park v. Volpe*, *supra* at 415-16, 91 S.Ct. at 824. Although the agency's decision is entitled to a presumption of regularity, this does not preclude a thorough, probing, in-depth review. *Citizens to Preserve Overton Park v. Volpe*, *supra* at 415, 91 S.Ct. 814.

Meaningful judicial review requires determining that an agency's course of action flowed from a proper interpretation of the relevant law and a proper application of that law to facts sufficiently well developed by agency inquiry as to reflect the truth of the matter in controversy. The court should intervene where it appears from a combination of danger signals, that the agency really has not taken a "hard look" at the salient problems, and has not *genuinely* engaged in reasoned decision-making.<sup>5</sup> *Greater Boston*

intent. This immersion in the evidence enables the court to determine whether the agency decision was rational and based on the relevant factors. *Ethyl Corp. v. Environmental Protection Agency*, 176 U.S.App.D.C. 373, 407-408, 541 F.2d 1, 35-36 (1976).

<sup>5</sup> Considerable evidence calls into question FDA's sense of objectivity in this case.

When this suit was initiated, FDA had declared Laetrile a "new drug" without ever having constructed an administrative record in support of such designation. *See Rutherford v. United States*, 424 F.Supp. 105 (W.D.Okl. 1977). Ideally, agency decisions and conclusions should flow from a probing and objective analysis of a carefully amassed and encompassing factual record. When ordered on remand to conduct an appropriate investigation, FDA begrudgingly announced its intentions to do so and then previous to ever having received the evidence on which its conclusions are ostensibly based,

*Television Corporation v. F.C.C.*, 143 U.S.App.D.C. 383, 393, 444 F.2d 841, 851 (1970).

The exercise of discretionary authority requires a decision based upon adequate information; to act without collecting necessary facts is abusive of discretion. *Xytex Corporation v. Schliemann*, 382 F. Supp. 50, 53 (D.Colo. 1974).

After collecting the facts, the appropriate legal standards must be applied.<sup>6</sup> If administrative construction of a statute is clearly wrong, it is the court's duty to correct.<sup>7</sup> *R. V. McGinnis Theatres and Pay*

FDA reaffirmed its same, entrenched positions on the salient issues in the case. *See* "Laetrile—Notice of Administrative Rule Making Hearing," (R 1) (42 Fed. Reg. 10066 (1977)). Understandably, many contributors to the administrative record expressed skepticism concerning the proceedings' fairness.

<sup>6</sup> "When an administrative officer is sitting in a dual role as judge of the law and trier of the facts, and when he, as judge, gives himself, as fact-finder, an incorrect instruction as to the law governing the decision he must make, error is committed just as there is error if a judge incorrectly charges a jury. We must assume that the examiner applied the standard as he stated it; and if he did, he erred, and on a question of law. The decision, therefore, cannot stand." *Williams v. Ribicoff*, 323 F.2d 231-32 (5th Cir. 1963).

<sup>7</sup> FDA errs as a matter of law when it asserts that Laetrile cannot escape new drug classification unless it is shown that: "It is currently intended *solely* for use under conditions prescribed recommended or suggested in its labeling on October 9, 1962." (emphasis supplied) Under this interpretation, if someone were suddenly to begin promoting aspirin for some new or unconventional purpose, all aspirin, regardless of its use, would ipso facto be subject to being classified a "new drug" and regulated as such under the provisions of the Act. The appropriate statutory construction requires that Laetrile

*T.V. v. Video Independent Theaters*, 386 F.2d 592, 594 (10th Cir. 1967), *cert. denied*, 390 U.S. 1014, 88 S.Ct. 1265, 20 L.Ed.2d 163 (1968). Administrative regulations must be consistent with the statute's purposes and reasonably adapted to carry out those purposes. *Greyhound Corporation v. United States*, 221 F.Supp. 440, 444 (N.D.Ill. 1963).

Having reviewed the Decision of the Commissioner of Food and Drugs on Laetrile, dated July 29, 1977,

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be considered exempt from "new drug" status *to the extent* that it is currently being used for the same purposes and under the same conditions and labeling as on October 9, 1962. The Act says that the 1962 "new drug" amendments "shall not apply to . . . [drugs] *when intended solely for use under conditions prescribed [October 9, 1962] . . .*" (emphasis supplied) Pub. L. No. 87-781 § 107(c) (4) (1962) *reprinted* at 21 U.S.C. § 321, n.

The term "labeling" is defined in the Act to include not only "all labels" but also "other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article. (21 U.S.C. § 321(m)) This definition has been given a broad interpretation, *see e.g. Kordel v. United States*, 355 U.S. 345, 347-50, 69 S.Ct. 106, 93 L.Ed. 52 (1948); *United States v. Urbuteit*, 335 U.S. 355, 357, 69 S.Ct. 112, 93 L.Ed. 61 (1948). Commissioner's Decision (R 523 at 143).

1962 labeling characterizes Laetrile as a palliative agent for use in "cancers beyond aid by standard agents," and warns that "it is not to be employed to the exclusion of surgery, radiation or similar standard modalities so long as they are indicated." Affidavit of Robert S. K. Young, Ph.D. (R 201 at H234) If "generally recognized as safe" by qualified experts, the "1962 grandfather clause" prevents Laetrile from being classified or treated as a "new drug" when labeled in substantially the same manner as previous to October 10, 1962. *See the "1962 Grandfather Clause" Issue*, p. 9.

(42 Fed.Reg. 39768-39806 (1977)), and the entire administrative record upon which that decision was based, and the pleadings and briefs, the court concludes that such decision is arbitrary, capricious, that it represents an abuse of discretion and is not in accordance with law. Consequently, it must be set aside and vacated. 5 U.S.C. § 706(2).

## ISSUES

The following issues are presented:

1. Is Laetrile a drug?
2. Is Laetrile a "new drug" within the meaning of § 201(p) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 321(p) in that it is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use in the cure, mitigation, treatment, or prevention of cancer in man, and in that it is not "grandfathered" by one of the Act's provisions applicable to those drugs marketed before the current "new drug" statutory provision became effective?
3. Is the agency action in question violative of plaintiffs' constitutional rights?

## NEW DRUG ISSUE

FDA asserts authority to preclude Laetrile's importation or interstate transportation on the basis that it is a "new drug" within the Act's meaning. "No person shall introduce or deliver for introduction into interstate commerce any new drug," unless an application on its behalf has been approved. 21 U.S.C. § 355(a). It is conceded that no such application in regard to Laetrile has been approved, but plaintiffs challenge the Commissioner's categorization of Laetrile as a "new drug."

Plaintiffs initially question the determination that Laetrile is a drug, contending instead that it is a vitamin or food. "Drug" is defined to include "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals . . . ." 21 U.S.C. § 321(g)(1)(B). The court need not rule whether Laetrile is a food or a vitamin, since, in any event, its well-recognized use in the treatment of cancer renders it a drug within the context of the statutory definition.<sup>8</sup>

<sup>8</sup> Numerous court decisions have emphasized that it is the intended use of an article which determines whether or not it is a "drug" and that even the most commonly ingested foods and liquids are "drugs" within the meaning of the Act if their intended use when distributed in interstate commerce falls within the definition of § 321(g)(1). See e.g. *Bradley v. United States*, 264 F. 79 (5th Cir. 1920) (mineral water); *United States v. "Vitasafe Formula M,"* 226 F.Supp. 266, 278

THE "GENERALLY RECOGNIZED . . .  
AS SAFE AND EFFECTIVE" ISSUE

If Laetrile's composition is such that it is generally recognized among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use in the treatment of cancer, it is not a "new drug" within the Act's meaning and not subject to the asserted FDA regulation. 21 U.S.C. § 321(p)(1).

Unquestionably, the administrative record in this case reveals a substantial and well-developed controversy among medical professionals and other scientists as to the efficacy of Laetrile.

Advocates of Laetrile's use in cancer treatment include many highly educated and prominent doctors

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(D.N.J. 1964) *remanded on other grounds*, 345 F.2d 864 (3rd Cir. 1965) *cert. denied*, 382 U.S. 918, 86 S.Ct. 290, 15 L.Ed.2d 232 (1965) (vitamin and mineral capsules); *United States v. 250 Jars . . . Fancy Pure Honey*, 218 F.Supp. 208, 211 (E.D. Mich. 1963) *affirmed*, 344 F.2d 288 (6th Cir. 1965) (honey); *United States v. 46 Cartons, etc.*, 113 F.Supp. 336, 338 (D. N.J. 1953) (cigarettes); *United States v. Research Laboratories*, 126 F.2d 42 (9th Cir. 1942), *cert. denied*, 317 U.S. 656, 63 S.Ct. 54, 87 L.Ed. 528 (1942); *Hanson v. United States*, 417 F.Supp. 30 (D.Minn. 1976) (Laetrile); *United States v. Article Consisting of 36 Boxes, etc.*, 284 F.Supp. 107 (D.Del. 1968) *affirmed*, 415 F.2d 369 (3rd Cir. 1969); *United States v. 3 Cartons, etc.*, 132 F.Supp. 569, 573 (S.D. Cal 1952).



and scientists<sup>9</sup> whose familiarity and practical experience with the substance vastly exceeds that of their detractors. To deem such advocacy "quackery"

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<sup>9</sup> Proponents of the use of Laetrile include:

Dean Burk, Ph.D., in biochemistry from the University of California. A research scientist possessing 35 years' experience with the National Cancer Institute, Dr. Burk is the former head of the Institute's Cytochemistry Section. (R 302; Tr. 401).

Charles Gurchot, Ph.D., in chemistry and physiology from Cornell University, former assistant professor of pharmacology, University of California Medical School at San Francisco. (R 302 at J-206).

Chauncey D. Leake, Ph.D., former associate professor of pharmacology at University of Wisconsin. (R 302 at J-200).

Raymond Ewell, Ph.D., in chemistry from Princeton. (R 302 at J-196).

Phillip Binzel, M.D., (Tr. 360); John A. Richardson, M.D. (R 510, Ex. 1 and Tr. 462); The Honorable Lawrence P. McDonald, M.D., Congressional Representative from the State of Georgia (R 509); Ernst T. Krebs, Sr., M.D., and Dr. Ernst T. Krebs, Jr., (Tr. 228); perhaps as many as 600 American M.D.'s or more have employed and are advocating the use of Laetrile in cancer treatment. (R 313 at J-255).

David Rubin, M.D., surgeon at Beilinson Hospital and cancer researcher at Hadassah Hospital in Jerusalem, Israel. (R 510, Ex. 12).

Mario A. Soto, M.D., of Mexico, authorized by the National Cancer Institute to conduct independent investigational studies with the Institute's cancer drugs. (R 286; Tr. 478).

Hans A. Nieper, M.D., Hannover, West Germany; Ernesto Contreras, M.D., Tijuana, Mexico; Shigeaki Sakai, M.D., of Tokyo, Japan; Ettore Guidetti, M.D., Brazil. (R 507).

Many doctors testify that Laetrile can confer an "improved quality of life" even upon patients who ultimately die, by reducing their pain and discomfort. For example, see P. E. Binzel, Jr., M.D., (Tr. 362); David Rubin, M.D. (R 510, Ex. 12.)

distorts the serious issues posed by Laetrile's prominence and requires disregarding considerable expertise mustered on the drug's behalf.

While the record reveals an impressive consensus among the nation's large medical and cancer-fighting institutions as to Laetrile's ineffectualness, a disconcerting dearth of actual experience with the substance by such detractors is revealed.

Special problems, medical, legal and philosophical, arise when applying the "generally recognized as safe and effective" standards of the Act to drugs employed in the treatment of cancer. There are many thousands of terminally ill cancer patients each year whose diseases have progressed to a point where, for them, no drug exists which can fairly be termed "generally recognized as safe and effective." These are the persons who have been told they are beyond help and have been sent home to die. Should further treatment of these people be precluded by the Act? Certainly not. Individuals for whom no orthodox cure is available surely are entitled to select a health-care approach with which they feel compatible.<sup>10</sup>

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<sup>10</sup> Not all members of America's leading cancer institutions are unalterably opposed in all context to Laetrile's use. "I have stated before, . . . that if the patient has exhausted the benefits of conventional treatment and does not mind the financial outlay, I see no harm in his taking Amygdalin in the way it has generally been used." Affidavit of C. Chester, Ph.D., vice-president and associate director for administrative and academic affairs of the Sloan-Kettering Institute for Cancer Research, New York. (R 195).

Nonetheless, while Laetrile's use in cancer treatment is widespread, its efficacy may, for statutory purposes, be inadequately documented. A drug can be "generally recognized" by experts as effective for intended use within the meaning of the Act only when that expert consensus is founded upon "substantial evidence" as defined in § 505(d), 21 U.S.C. § 355(d). *Weinberger v. Hynson, Westcott & Dunning, supra*, 412 U.S. at 632, 93 S.Ct. 2469.<sup>11</sup>

The current debate is fierce. The issue appears largely unresolved as to Laetrile's true effectiveness, in large part because FDA has prevented adequate testing on humans. Nevertheless, the evidence of record does not render the Commissioner's conclusion that Laetrile is not "generally recognized as safe and effective" arbitrary and capricious.

Significantly, however, a drug not recognized as safe and effective still "shall not be deemed to be a 'new drug' if at any time prior to [this] enactment [October 10, 1962] . . . it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same represen-

<sup>11</sup> "[T]he term 'substantial evidence' means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed . . ." 21 U.S.C. § 355(d).

tations concerning the conditions of its use . . ." 21 U.S.C. § 321(p)(1).<sup>12</sup>

Many believe that simply administering Laetrile to tumor-bearing mice, particularly when the results of such tests are so much in controversy,<sup>13</sup> is not dispositive of the issue. Laetrile proponents often submit that it should be utilized in conjunction with a dietary

<sup>12</sup> "The effect of this definition is that there is a twofold grandfather clause exemption which is capable of removing Laetrile from the new drug category even if it is not recognized by the experts as being safe and effective which, by the way, does not say it is unsafe and ineffective. The first of these grandfather exemptions comes from transitional provisions attached to the 1962 Amendments to the Food, Drug and Cosmetic Act of 1938. The second grandfather exemption arises from provisions attached to the 1938 Act when it superseded the original Food and Drug Act of 1906." *Rutherford v. United States*, 542 F.2d 1137, 1141 (10th Cir. 1976).

<sup>13</sup> Knowledgeable experts have expressed sharp criticism of certain prominent Laetrile tests on animals in which the substance was determined ineffective. Note the analyses of Dr. Bernard Kenton of the City of Hope National Medical Center, Los Angeles, California. (R 507 at N249); and Dr. Dean Burk (R 302 at J-117) also those of Dr. Michael Fox, chairman of the Biomathematics Department of the City of Hope National Medical Center, and assistant professor of biomathematics at UCLA, and Harold Hornsby, research scientist with NASA and a Fellow of the Royal Statistical Society in London (R 313 at J-253 and 254). Sloan-Kettering researcher Dr. Kanematso Sugiura performed at least six different tests in which he concluded that Laetrile was effective in combatting certain types of tumors; the Institute subsequently released other test results reportedly contradicting Dr. Sugiura's findings. Dr. Sugiura is quoted as saying: "It is still my belief that amygdalin cures metastases." (R 313 at J-241).



regimen essential to the drug's success.<sup>14</sup> Significantly, animal testing sheds little light on the placebo effect, that is, the healing effect accompanying the psychological uplift and renewed sense of hope which often attends administration of a substance in which a patient strongly believes.<sup>15</sup> It is only when the substance is openly used, and its results carefully observed and fully reported that this controversy will be resolved.

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<sup>14</sup> "I know of no doctor throughout the world who is now using Amygdalin who does not agree that the maximum benefit from Amygdalin is obtained when it is used in combination with other vitamins, enzymes and proper diet." P. E. Binzel, Jr., M.D. (Tr. 363).

<sup>15</sup> "Humans are very susceptible, particularly when ill and desperate with hope to the power of positive suggestion—namely, when given a 'drug' by an authority figure (e.g., a physician) with the firm statement and promise they will now begin to feel better, to have pain relief, to eat better, and to get well, these hopeful patients frequently do just what they have been told to expect. This effect has long been recognized in medicine and is termed 'placebo effect.'" Affidavit of Daniel S. Martin, M.D. (R 185 at 7). One noted expert argues: "... the only way to achieve the placebo effect, itself, is for some authority to indicate that the drug could be effective. There is no official, no ethical way to do that." R. Lee Clark, M.D., president of the American Cancer Society. (R 307 at J-228). The record clearly reveals, however, that many doctors are convinced that Laetrile is capable of playing a legitimate and significant role in the treatment of cancer, and are perfectly willing to administer it on that basis. See n. 6.

## IV

## THE "1962 GRANDFATHER CLAUSE" ISSUE

If on October 9, 1962, Laetrile was marketed for the same uses for which it is presently being sold and if generally recognized by qualified experts as safe for those uses, the grandfather clause exempts it from the test of general recognition by experts as being both safe and effective for its claimed uses. *Rutherford v. United States*, 542 F.2d 1137 (10th Cir. 1976) *supra*; *Tyler Pharmacal Distributors, Inc. v. United States Department of HEW*, 408 F.2d 95, 99 (7th Cir. 1969).<sup>16</sup>

Based upon FDA's own administrative record in this case and the applicable statutes and case law, the court concludes that the agency's classification of

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<sup>16</sup> "One of the transitional provisions enacted in 1962 was as follows:

'In the case of any drug which, on the day immediately preceding the enactment date (October 10, 1962), (A) was commercially used or sold in the United States, (B) was not a new drug as defined by Section 201(p) of the basic Act as then in force (21 U.S.C. Section 321(p)), and (C) was not covered by an effective (new drug) application under 505 of that Act (21 U.S.C. Section 355), the amendments to Section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day. Pub. L. 87-781, Section 107(c) (4), reprinted at 21 U.S.C. Section 321 note.'" *Rutherford v. United States*, (10th Cir. 1976 *supra*, 542 F.2d at 1141.)

Laetrile<sup>17</sup> as a "new drug" is "arbitrary, capricious,

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<sup>17</sup> The Commissioner's report concludes that the terms "Laetrile" and "Amygdalin" do not refer to the same substance and cannot be used interchangeably. Such report assigned to Amygdalin the chemical formula of D-mandelonitrile-beta-D-glucoside-6-beta-D-glucoside, while assigning to Laetrile, on the basis of a formula derived by Dr. Ernst T. Krebs, Jr., the designation 1-mandelonitrile-beta-glucuronic acid. The record reveals that the latter formula has reference to a theoretical model that Krebs developed but apparently either never synthesized or never chose to employ to any material extent. (R 183) The substance in controversy in this case, and with which this opinion is concerned, is described by the first formula; as recognized by the Commissioner, Laetrile's proponents and opponents alike refer to the substance both as "Amygdalin" and "Laetrile." Such substance is that same Amygdalin or Laetrile to which the Commissioner made reference in his "Laetrile—Notice of Administrative Rule Making Hearing" (42 Fed. Reg. 10066 (1977)) when he stated: "Laetrile is the name of a product whose major component or ingredient is the chemical amygdalin, a substance that occurs naturally in the pits of apricots, peaches, bitter almonds and in other plant material . . ." and it ". . . has been known, tested, and used [as a cancer remedy] for more than 25 years . . . ."

Numerous judicial determinations have been made equating Laetrile and Amygdalin. See *United States v. Spectro Foods, Corp.*, Civ-76-101, (Dist.N.J. 1976) *affirmed in part reversed in part*, 544 F.2d 1175 (3rd Cir. 1976); *United States v. General Research Laboratories*, 397 F.Supp. 197 (C.D.Cal. 1975); *Rutherford v. United States*, 399 F.Supp. 1208, 1211 (W.D. Okl. 1975), 424 F.Supp. 105-06 (W.D.Okl. 1977).

The administrative record clearly establishes that Laetrile and Amygdalin are equivalent and have been recognized as such for over 20 years. The American Cancer Society, in a pamphlet entitled "Questions Most Frequently Asked About 'Laetrile'," answered in response to the question, "What is Laetrile?": "The scientific name of the drug is amygdalin; 'Laetrile' is a registered trade mark." (R 173 at 144D) Frank

an abuse of discretion" and as a matter of law unsupportable. *Citizens to Preserve Overton Park v. Volpe, supra*, 401 U.S. at 416, 91 S.Ct. 814; 5 U.S.C. § 706(2) (A).

The record and the law reasonably support but one conclusion: Laetrile (Amygdalin) has been commercially used and sold in the United States for the treatment of cancer for well in excess of 25 years, during

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J. Rauscher, Jr., Ph.D., Director of the National Cancer Program for the National Cancer Institute equates Laetrile with Amygdalin in his "Statement Concerning Laetrile." (R 173 at 222D) So too does Dean Burk, Ph.D., former head of the Cytochemistry Section of the National Cancer Institute (R 302 at J-60, J-71); Raymond Ewell, Ph.D., former professor of chemistry at the State University of New York at Buffalo (R 302 at J-196); Thomas H. Jukes, Ph.D., professor in residence in medical physics and research biochemist, University of California at Berkeley. (R 416 at M-77-78).

The affidavit of W. Sherwood Lawrence, M.D., a medical officer of the Department of Health of the State of California, the Executive Secretary of the State of California Cancer Advisory Council, and a Laetrile opponent, clearly establishes Laetrile and Amygdalin as being one and the same. (R 183).

Numerous "official samples" of Laetrile collected by the State of California over a period of years and chemically analyzed have established the substance as Amygdalin. Analysis by the AMA of the Laetrile employed by the originators of the term, Drs. Ernst T. Krebs, Sr. and Jr., determined the substance to be Amygdalin, as did the 1953 report on Laetrile by the Cancer Commission of the California Medical Association. The report stated: "Chemical analyses done independently for the Commission have identified in the product distributed as Laetrile only the presence of a natural Laetrile termed Amygdalin." (R 183 at 29F) The testimony of both Drs. Krebs also clearly establishes this fact. (R 183 at 196F; Tr. 228).

which time it has been "generally recognized" by qualified experts as safe<sup>18</sup> for such use.

<sup>18</sup> The issue of Laetrile's *safety* possesses several different facets. FDA contends that even if Laetrile were marketed prior to 1962 it must be shown to have been "effective" as well as "safe" since it was used in the treatment of a "life-threatening disease," cancer, and thus was not safe if ineffective. Commissioner's Decision (R 523 at 189). Such legal premise could be extended to abrogate all distinction between the terms "safe" and "effective" and is unmeritorious; any ineffective remedy may displace an effective one, regardless of the disease's severity, and in that sense is unsafe. The Supreme Court in *Weinberger v. Hynson, supra*, stated that "the 1962 amendments [of the Food, Drug and Cosmetic Act] for the first time gave FDA power to scrutinize and evaluate drugs for *effectiveness as well as safety*." 412 U.S. 630, 93 S.Ct. 2483 (emphasis supplied). In any event, FDA's argument "may lose its force in the case of a terminally-ill patient or in the case of a patient suffering from a disease for which there are no 'effective' remedies." *Rutherford v. United States*, (10th Cir. 1976), *supra*, n. 5, 542 F.2d at 1142. FDA erred as a matter of law when it determined that a cancer drug cannot be "grandfathered" on the basis of pre-1962 use unless shown to be effective as well as safe. As to the danger that Laetrile's use results in postponement of conventional treatments to the patient's detriment, it is to be noted that outlawing Laetrile has not resulted in disuse but merely in large numbers of Americans traveling to Mexico. It has been estimated that each year 20,000 Americans afflicted with cancer travel to Mexico to receive Laetrile treatments. (R 313 at J-242) Thus Laetrile's illegality actually tends to remove many patients from the care of their American doctors.

As to selecting Laetrile over orthodoxy, the record discloses that the vast majority of Laetrile patients first underwent the relevant conventional treatments. While isolated, tragic instances may have occurred in which Laetrile was used and conventional treatments avoided, to a patient's detriment,

Amygdalin was reportedly first isolated from bitter almonds by the French Chemists Robiquet and Burton-Charland in 1830. The name "Amygdalin" was derived from the word "Amygdala," Greek for almond. Commissioner's Decision. (R 523 at 23).

Reports of its employment in the treatment of cancer were first published in 1845 and 1846.<sup>19</sup>

In 1949 doctors utilizing Amygdalin as a cancer treatment in the United States coined the term "Laetrile."<sup>20</sup>

Extensive use of the substance, its commercial availability,<sup>21</sup> and its recognition as being safe, all

such persons might well have opposed orthodox approaches and remained untreated even were Laetrile unavailable.

Too, Laetrile may be administered either parenterally or orally; the latter method, some contend, is more dangerous than the former. While the record discloses certain differences of opinion on this issue, the vast amount of practical experience of actual experimenters and users, in administering Laetrile both parenterally and orally, has established its non-toxicity. See n. 15; also see Tr. 311. One journalist reports that 50,000 American cancer patients are currently using over 1 million grams of Laetrile per month. (R 507).

<sup>19</sup> J. D. Inosemtzoff, in *Gazette Medicale de Paris*, No. 37 September 13, 1845, pp. 577-582; *Journal Chirurgie/Augenheilkunde* 1846. (R 302, Ex. A, at J-65).

<sup>20</sup> "In 1949, my son, Ernst T. Krebs, Jr. gave the name Laetrile to the Amygdalin I was producing and I have used the name of Laetrile ever since that time for the final form of the Amygdalin which I produce." Affidavit of Ernst T. Krebs, Sr., M.D. (Apr. 1965) (R 183 at 196F).

<sup>21</sup> "Use of a drug is investigational, as contrasted with commercial, when that use is for the purpose of determining



previous to 1962, are well-documented in the record.

Any restrictions placed on the commercial availability or use of Laetrile by FDA previous to July 29, 1977, when the administrative record and Commissioner's Decision were filed, were unsupported by any competent administrative record whatsoever and subject to attack as a matter of law.<sup>22</sup>

The administrative record brooks little real controversy as to Laetrile's nontoxicity, particularly when

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whether, or demonstrating that, the drug in question is safe and effective." Commissioner's Decision. (R 523 at 168).

While the record reveals many instances of investigational use of Laetrile, extensive use of the substance as a part of various doctors' fundamental regimen in treating cancer is also demonstrated.

The record's whole tenor reasonably establishes the commercial availability of Laetrile (Amygdalin) during the period in question. As noted earlier, the substance was extracted well over a century ago and has long been pharmaceutically recognized. "Of my own personal knowledge, I know that both prior and subsequent to 1938 amygdalin was readily available to anyone who wanted it from United States suppliers of chemicals . . . [and that] amygdalin was listed and is still listed, as a purchasable item in various chemical catalogs published in the United States." Charles Gurchot, Ph.D. in chemistry. (R 302 at J-211).

Several documents in the record allude to a controversy in California in the early 1950's over variations in the price of Laetrile (Amygdalin) among sellers. (R 183 at 105F-111F) Note for example the letter from N. Schneider of Van, Waters & Rogers, Inc., which clearly establishes the commercial availability of Amygdalin between 1952 and 1964. (R 183 at 108F).

<sup>22</sup> See *Rutherford v. United States* (10th Cir. 1976), 542 F.2d 1137 *supra*; *Rutherford v. United States*, 424 F.Supp. 105 (W.D.Okl. 1977); and the record from the December 30, 1976, "Hearing to Implement Tenth Circuit Court Ruling" pp. 13-14.

administered parenterally, even at doses greatly exceeding amounts normally ingested.<sup>23</sup>

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<sup>23</sup> In the only laboratory study of record specifically designed to determine the drug's toxicity, it was observed: "Amygdalin, at all doses studied, appears to be completely non-toxic in laboratory mice." Harold W. Manner Ph.D., Chairman, Department of Biology, Loyola University, Chicago, Illinois (R 262). Of the various controversial tests studying Laetrile's efficacy on animal tumors, none have disclosed toxicity at reasonable dosage levels.

Among the numerous scientists and physicians testifying from first-hand experience with Laetrile and its effect on humans, unanimity exists as to its nontoxicity.

Dr. Phillip Binzel, M.D., graduate of St. Louis University, testified that he has personally given nearly 4,000 intravenous injections of Amygdalin using doses up to 9 grams without any adverse reaction. (Tr. 363).

Daniel S. Martin, M.D., who participated in the same Sloan-Kettering experiments in which Dr. Sugiura detected cancer inhibiting properties in Laetrile, and who disputed Dr. Sugiura's results, nonetheless concluded that there was no doubt that Laetrile was nontoxic, at least if administered parenterally. (Tr. 437).

Charles Gurchot, Ph.D., testified for the record in affidavit form that Amygdalin in liquid and solid form was used prior to 1962 (between 1934 and 1945) by Gurchot, under the supervision of five named medical doctors at the University of California Medical School at San Francisco. This Amygdalin was, according to his statement, administered "on patients intramuscularly and intravenously." He further stated that during this same period Amygdalin was being used to his personal knowledge by approximately a dozen California physicians in their treatment of cancer. Gurchot expressed his belief that Amygdalin was generally recognized by experts as being safe for use in the treatment of cancer on or prior to October 10, 1962. (R 302 at J-206).

Chauncey D. Leake, Ph.D., indicated in his affidavit that he is familiar with Dr. Gurchot's use of Amygdalin in the mid 1930's and 1940's at the University of California Medical

School Hospital in San Francisco. He further indicates that physicians and other scientists familiar with Amygdalin recognized it as safe at that time. (R 302 at J-200).

Dr. Dean Burk, former head of the Cytochemistry Section, National Cancer Institute, Bethesda, Maryland, after testing Amygdalin on rats, says the substance is "notably less toxic to animal organisms than ordinary diet sugar," and that aspirin tablets are 20 times more toxic than an equivalent amount of Amygdalin. (R 183 at 166F).

"Investigators have found that intravenous doses in excess of 20 grams have been without toxic effect in healthy human subjects, although occasionally a mild hypotensive effect may be observed. Repeatedly, studies have indicated that pure Amygdalin, when administered parenterally is astonishingly devoid of toxic effects." (R 183 at 166F).

Donald C. Thompson, M.D., of Morristown, Tennessee, testified as to his personal experience with administering Laetrile to patients and affirmed the drug's nontoxicity. (R 515).

In his report entitled "Use of Laetrile in the Prevention and Treatment of Cancer," Dr. David Rubin, M.D., surgeon at Beilinson Hospital and cancer researcher at Hadassah Hospital in Jerusalem, Israel, asserts: "Laetrile is nontoxic even in very large injected doses." (R 510, Ex. 12).

As another example of a practicing physician who has extensively used Amygdalin and determined it to be nontoxic, see the letter of The Honorable Lawrence P. McDonald, Congressional Representative from Georgia. (R 509 at N265-68).

"Amygdalin (Laetrile) is totally non-toxic systemically, at commonly applied dosages." Hans A. Nieper, M.D., Hannover, West Germany. (R 302 at J-180).

While a doctor's inability to control many variables potentially relevant to curing a disease may impugn the credibility of his perceptions as to a drug's efficacy (see *Weinberger v. Hynson, supra*) his observations as to its toxicity are much more reliable, since the relevant variables are more manageable.

"(Laetrile) is totally nontoxic. Its lethal dose in mice and rats, by injection, is about 25,000 milligrams per kilogram of body weight. It is so nearly nontoxic that in some studies the water, used as a dilutant presents a greater toxicity than the

Interestingly, however, Laetrile's candidacy for exemption from "new drug" status rests less on its "safeness" in fact than on its "generally recognized" reputation in that regard among qualified experts. *Durovic v. Richardson*, 479 F.2d 242, 250 (7th Cir. 1973). The record clearly reflects that previous to 1962 Laetrile was generally recognized as safe.<sup>24</sup>

vitamin." *The Journal of Applied Nutrition*, Ernst T. Krebs, Jr. (R 302 at J-187).

". . . All the available facts indicate that Amygdalin is essentially non-toxic to laboratory animals and to humans." Raymond Ewell, Ph.D. in chemistry from Princeton, retired professor from the State University of New York at Buffalo. (R 302 at J-196).

<sup>24</sup> "Among experts qualified by scientific training and experience to evaluate the safety of chemical substances in drugs, it is my information and belief that at least since the 1930's pure amygdalin has been generally recognized as safe for use by human beings either by injection, intravenously or intramuscularly, or by oral intake. For example, pure amygdalin may be administered without adverse effect in amounts of 10 grams per day, orally or 3 grams intravenously to a 150 pound man. . . ." Charles Gurchot, Ph.D. (R 302 at J-211 and 212).

The authoritative publication, *The Dispensatory of the United States* (1950 ed. p. 40) emphasizes that "Amygdalin itself is practically non-toxic . . . ." *Synopsis of Materia Medica, Toxicology and Pharmacology*, C. V. Mosby Company, 1944, p. 33, affirms that "the glucoside Amygdalin, given by injection, produces no harmful effects." (R 183 at 166F).

"With 45 years of study and research on the cancer problem, . . . I have found no statements of data on demonstrated, sustained pharmacological harmfulness to human beings of amygdalin at any dosages recommended or employed by physicians in the United States and abroad, up to the high level of 200 milligrams per kilogram of body weight per day (equals 15 grams-75 kilogram man-day), administered either

orally or parenterally; and, more specifically no such statements by official opponents of the use by humans of amygdalin, including comment in their major publications. Few substances have been so widely investigated regarding nontoxicity and chemical definition as has amygdalin, by pharmacologists and chemists in many countries of the world, for over 125 years. . . . Amygdalin has been known and widely recognized for over one hundred years as nontoxic for man." Dean Burk, Ph.D., from the pamphlet *Vitamin B-17 . . . a Brief on Foods and Vitamins*. (R 302 at J-69 and J-65).

In its 1963 "Report on the Treatment of Cancer With Beta Cyanogenetic Glucosides ('Laetriles')" the only potential danger discerned by the Cancer Advisory Council of the State of California was "that the use of one or more of these substances in early cancer, to the exclusion of conventional treatment might well be dangerous since treatment with acceptable, curative methods (surgery or radiation) would thereby be delayed potentially until such time as metastases were manifest and the cancer might therefore no longer be curable. (R 183 at 246F) No toxicity was reported in the 1953 case study report of the Cancer Commission of California Medical Association.

It is only within the context of FDA's creation of this record that the specter of Laetrile's toxicity has even been raised. The drug's reputation for nontoxicity, even among its opponents, is amply documented. See, for example: "Harmless, but Ineffective Remedies," *The Journal of Pharmaceutical Sciences*, Oct., 1975. (R 180 at 190E) FDA allegations of toxicity appear to be more of an afterthought offered to bolster their other conclusions, rather than a reasoned conclusion based on a detached, impartial view of the record.

While apricot kernels can be poisonous if ingested in very large quantities, such contain enzymes not present in Amygdalin; thus, the toxicity of apricot kernels and Amygdalin are not comparable. Deposition of Raymond Ewell, Ph.D. (R 302 at J-197).

## V

## THE "1938 GRANDFATHER CLAUSE" ISSUE

An added ramification of the Act's grandfather clause is that a drug may escape the "new drug" machinery if it was marketed or officially recognized as a drug at any time before June 25, 1938, but after June 30, 1906, if the prescribed conditions for its use are unchanged. Thus, if Laetrile were marketed or officially recognized during those years as a cancer drug, it would not be subject to "new drug" instrumentalities of the 1962 amendments even though not generally recognized as safe or effective. *Rutherford v. United States*, (10th Cir. 1976) *supra*, 542 F.2d at 1142.

While Amygdalin (Laetrile) was indeed employed in combatting cancer previous to 1938, the record fails to establish the details of its use during that period sufficiently to successfully challenge FDA's denial of this exemption.

## VI

## "CONSTITUTIONAL ISSUES"

In plaintiffs' constitutional challenge of FDA's prescription they invoke rights fundamental to a free society and inextricably related to enumerated constitutional concepts.

While the Constitution does not explicitly mention a right of personal privacy, it is unchallengeable "that a right of personal privacy, or a guarantee of



certain areas or zones of privacy, does exist under the Constitution.” *Roe v. Wade*, 410 U.S. 113, 152, 93 S.Ct. 705, 726, 35 L.Ed.2d 147 (1973). This right has been discerned within the penumbras of the Bill of Rights, and specifically within the language of the First, Fourth, Fifth, Ninth and Fourteenth Amendments to the Constitution, *Roe v. Wade, supra*. “. . . only personal rights that can be deemed ‘fundamental’ or ‘implicit in the concept of ordered liberty,’ . . . are included in this guarantee of personal privacy.”

Mr. Justice Douglas referred to “the freedom to care for one’s health and person” as coming within the purview of this right. *Doe v. Bolton*, 410 U.S. 179, 213 (1973), 93 S.Ct. 739, 758, 35 L.Ed.2d 201 (concurring opinion). “The right of privacy,” Justice Douglas proceeded, “has no more conspicuous place than in the physician-patient relationship . . .” *Doe, supra* at 219, 93 S.Ct. at 761. He concluded: “The right to seek advice on one’s health and the right to place reliance on the physician of one’s choice are basic . . .” *Doe, supra*.

This right of privacy has been characterized more than once as simply the right “to be let alone.” *Doe v. Bolton, supra*, at 213, 93 S.Ct. 739 (Justice Douglas concurring); *Olmstead v. United States*, 277 U.S. 438, 478, 48 S.Ct. 564, 72 L.Ed. 944 (Justice Brandeis dissenting). That right includes the privilege of an individual to plan his own affairs, for “‘outside areas of plainly harmful conduct, every American is

left to shape his own life as he thinks best, do what he pleases, go where he pleases.’” *Kent v. Dulles*, 357 U.S. 116, 126, 78 S.Ct. 1113, 1118, 2 L.Ed.2d 1204; *Doe v. Bolton, supra* 410 U.S. at 213, 93 S.Ct. 739, 758 (concurring opinion).

Many knowledgeable and concerned individuals are questioning the effectiveness and wisdom of our orthodox approaches to combatting cancer. The correctness of their criticisms may not be determined for many years, and in any event such discussion provokes controversies largely beyond the realm of the courts’ function. Nonetheless, it appears uncontroversial that a patient has the right to refuse cancer treatment altogether, and should he decide to forego conventional treatment<sup>25</sup> does he not possess a fur-

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<sup>25</sup> Such a decision is by no means necessarily indicative of suicidal tendencies. Dr. Hardin Jones of the University of California has presented impressive evidence in support of the thesis that in some instances at least untreated cancer victims outlive treated ones. (R 507) Conventional modes of treatment, particularly radiation and chemotherapy, can cause extensive damage to healthy organs and tissues as well as cancerous ones. Some argue that in destroying the body’s natural defense mechanisms such approaches often destroy important weapons crucial to an effective fight against cancer and also greatly increase a patient’s vulnerability to other life-threatening diseases as well.

Patients possessing particularized complicating factors, such as old age, frail physical constitutions, or certain types of religious convictions, might also understandably decide to forego the rigors of such conventional methodologies.

Even doctors who oppose the use of Laetrile will generally concede as to orthodox modes of treatment (surgery, radiation and chemotherapy): “. . . the treatments that are available are very often disfiguring; they can be painful; they can be

ther right to enlist such nontoxic treatments, however unconventional, as he finds to be of comfort, particularly where recommended by his physician?

We must carefully distinguish between the constitutional standards applicable to the use of an innocuous substance as a health-care aid, and those standards which apply to the promotion or advertisement of that same substance.

Plaintiffs seek to exercise final control over the handling of their own individual health-care problems. Numerous cancer patients possess extensive first-hand experience with Laetrile which has led them to believe, correctly or not, that the substance has eased their pain and prolonged their lives. Such personal convictions are not readily dispelled by government pronouncements or affidavits to the con-

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unpleasant; they can even be risky." Emil J. Freireich, Professor of Medicine at the University of Texas, School of Medicine, Houston. (Tr. 204)

In attacking the credibility of "cures" reported to have been effectuated by Laetrile, FDA argues that in many such instances the person involved may never even have had cancer. "Even where the diagnosis has been done by someone other than a Laetrile proponent, a mistake is possible. Some cancers which are discussed in reference to Laetrile are very difficult to diagnose histologically. Thus, a diagnosis of cancer may often on later review be reversed." Commissioner's Decision (R 523 at 227) This analysis is hardly reassuring to individuals such as plaintiff Glen Rutherford, whose proposed surgery, a colostomy, would have unalterably lessened the quality of his life, irrespective of the ultimate outcome of his illness. (*See Rutherford v. United States*, 399 F.Supp. 1208 (W.D.Okl. 1975).)

trary.<sup>26</sup> When deprived of treatment in this country, they go elsewhere, and in so doing are denied close contact with their families and family doctors.

Unintentionally FDA has wrought needless hardship and expense to countless individuals required to travel to Mexico or Germany in order to utilize Laetrile. If it were more readily available in this country, perhaps many patients currently obtaining the treatment abroad could be persuaded to remain under their doctor's care here and use the substance in conjunction with conventional treatments.

The final consequences are ultimately borne by those whose bodies are the battleground on which cancer's war is waged. Many perceive the drug's acquisition as a life and death matter, and are understandably frustrated and enraged over attempts by their own government to deny them the right to decide for themselves questions of such a personal and grave nature.

Doubtless FDA desires to protect the public. Such good intention, however, is not the overriding issue. Many of us allocate time and money and other resources in ways susceptible to just criticism by many standards. Nonetheless, our political ideals emphasize that the right to freely decide is of much greater significance than the quality of those choices actually made. It is never easy for one who is concerned and feels himself particularly knowledgeable to observe

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<sup>26</sup> "There can be few patients taking Laetrile in this country today who do not know that the government and most experts consider it worthless." Commissioner's Decision (R 523)



others exercise their freedom in ways that to him appear unenlightened.

As a nation, however, historically and continuously, we are irrevocably committed to the principle that the individual must be given maximum latitude in determining his own personal destiny.

To be insensitive to the very fundamental nature of the civil liberties at issue in this case, and the fact that making the choice, regardless of its correctness, is the sole prerogative of the person whose body is being ravaged, is to display slight understanding of the essence of our free society and its constitutional underpinnings. This is notably true where, as here, there are no simple answers or obvious solutions, uncertainty is pervasive, and even the best efforts leave so much to be desired.<sup>27</sup>

When certain "fundamental rights" are invoked, such as the right of privacy involved herein, regulation may be justified only by a "compelling state interest," and legislative enactments "must be narrowly drawn to express only the legitimate state in-

<sup>27</sup> 1977 *Cancer Facts and Figures* by the American Cancer Society estimates that 1977 will have produced an estimated 690,000 new cancer cases; and that over 54 million Americans now living will eventually have cancer, which is one out of every four Americans living. The pamphlet also states that over the years cancer will strike in approximately two of every three families, that in the 1970's there will be an estimated 3.5 million cancer deaths, 6.5 million new cancer cases, and more than 10 million people under medical care for cancer. Only about 1/3 of all people who get cancer this year will be alive five years after treatment, according to the publication. (R 173 at 113D)

terests at stake." *Roe v. Wade, supra*, 410 U.S. at 155, 93 S.Ct. at 728. By denying the right to use a nontoxic substance in connection with one's own personal health-care, FDA<sup>28</sup> has offended the constitutional right of privacy.

This court's decision in this case in no way portends the return of the traveling snake oil salesman. As emphasized earlier, the right to use a harmless, unproven remedy is quite distinct from any alleged right to promote such. FDA is fully empowered under other statutory provisions to combat false or fraudulent advertising of ineffectual or unproven drugs. See the Food, Drug and Cosmetic Act, Misbranded Drugs and Devices, 21 U.S.C. § 352 (1976); and the Federal Trade Commission Act, Dissemination of False Advertisements, 15 U.S.C. § 52 (1975).

The Commissioner's "Laetrile" Decision of July 29, 1977, must be vacated. An appropriate Order will accordingly be entered herein.

## ORDER

This action came on for determination by the court, and the issues having been duly considered and a

<sup>28</sup> Even if no such right existed generally, it would appear that Laetrile's use by terminally ill cancer patients who have exhausted orthodox approaches of cancer patients interested in using Laetrile only in conjunction with conventional methods would be constitutionally protected. While certain problems may attend exact definitions of "terminally ill," the term has a well understood meaning and is of practical significance to our discussion.

decision having been duly rendered as set forth in the Opinion of even date herewith,

IT IS ORDERED, ADJUDGED AND DECREED:

1. The action of the Commissioner of Food and Drugs dated July 29, 1977, is declared unlawful and such action, findings and conclusions are hereby vacated, set aside and held for naught;

2. Laetrile (Amygdalin) is exempt from the "new drug" requirements of 21 U.S.C. § 355(b);

3. The Secretary of Health, Education and Welfare and his subordinates in the Food and Drug Administration are hereby permanently enjoined and restrained from interfering, directly or indirectly, or acting in concert with United States Customs Service or others, with the importation, introduction, or delivery for introduction into interstate commerce by any person of Laetrile (Amygdalin) for the reason that application has not been filed or approved in the manner provided by 21 U.S.C. § 355(b) for a "new drug";

4. The Secretary of Health, Education and Welfare and his subordinates in the Food and Drug Administration are hereby permanently enjoined and restrained from interfering with the use of Laetrile (Amygdalin) for the care or treatment of cancer by a person who is, or believes he is, suffering from the disease;

5. The Secretary of Health, Education and Welfare and his subordinates in the Food and Drug Administration are hereby enjoined and restrained from

interfering with any licensed medical practitioner in administering Laetrile (Amygdalin) in the care or treatment of his cancer patients;

6. The Secretary of Health, Education and Welfare shall distribute or cause to be distributed to all personnel within the Food and Drug Administration and the United States Customs Service concerned or involved in the enforcement of the Food and Drug Act copies of the Opinion and Order herein, and shall file with the Clerk of this Court within twenty (20) days of the date hereof his certificate showing distribution as required herein;

7. This Order is binding upon the Secretary of Health, Education and Welfare, his agents, servants and employees in the Food and Drug Administration, present and future, and upon those persons in active concert or participation with them who receive actual notice of this Order by personal service or otherwise;

8. The Clerk of this Court shall serve by certified mail, deliver to addressee only, return receipt requested, Joseph A. Califano, Secretary of Health, Education and Welfare; Donald Kennedy, Commissioner of the Food and Drug Administration; and Vernon D. Acree, Commissioner of the U.S. Customs Service and their attorneys of record, certified copies of the Opinion and Order herein;

9. The Court hereby retains jurisdiction for all further orders appropriate and necessary to enforce this Order or to adjudicate any dispute arising here-

under. Any complaints arising under this Order by any party shall be heard by the Court on not less than five (5) days notice to the opposing party.

**APPENDIX E****DEPARTMENT OF HEALTH, EDUCATION,  
AND WELFARE**

Food and Drug Administration

[Docket No. 77N-0048]

**LAETRILE**

Commissioner's Decision

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Commissioner of Food and Drugs announces that he has compiled a comprehensive administrative record containing information about the drug Laetrile in general and, specifically, about two issues concerning Laetrile's "new drug" status: (1) Whether Laetrile is generally recognized by qualified experts as a safe and effective cancer drug, and (2) whether Laetrile is exempt from the premarket approval requirements for new drugs by virtue of the "grandfather" provisions of the Federal Food, Drug, and Cosmetic Act. The Commissioner concludes, after careful review of this administrative record, including oral argument presented at a public hearing, that: (1) Laetrile is not generally recognized by qualified experts as a safe and effective cancer drug, and (2) Laetrile is not exempt from the premarket approval requirements for new drugs by virtue of



the "grandfather" provisions of the act. Distribution of Laetrile in interstate commerce is thus illegal and subject to regulatory activity by the Food and Drug Administration. Conclusions on other issues related to the controversy concerning Laetrile are also set out.

EFFECTIVE DATE: August 5, 1977.

ADDRESSES: The transcript of oral argument presented at the public hearing, affidavits, written testimony, and all other submissions compiled as the administrative record for this proceeding may be seen in the office of the Hearing Clerk (HFC-20), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857, between 9 a.m. and 4 p.m., Monday through Friday. In addition, one copy of the administrative record (except two videotapes of interviews with cancer patients who had been treated with Laetrile) is available for public examination at the following Food and Drug Administration offices during regular business hours: 850 Third Ave., Brooklyn, NY 11232; 880 W. Peachtree St., Atlanta, GA 30309; 433 W. Van Buren St., Chicago, IL 60607; 1009 Cherry St., Kansas City, MO 64106; 1521 W. Pico Blvd., Los Angeles, CA 90015; 909 First Ave., Seattle, WA 98104.

#### FOR FURTHER INFORMATION CONTACT:

Tenny P. Neprud, Compliance Regulations Policy Staff (HFC-10), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3480.

SUPPLEMENTARY INFORMATION: In a notice published in the FEDERAL REGISTER of February 18, 1977 (42 FR 10066), the Commissioner announced that he was initiating a rulemaking proceeding to comply with the opinion of the Court of Appeals in *Rutherford v. United States*, 542 F.2d 1137 (10th Cir. 1976), and the order of the District Court in *Rutherford v. United States*, 424 F. Supp. 105 (W. D. Okla. 1977). In those proceedings, the Food and Drug Administration (FDA) was ordered to develop an administrative record concerning the following two issues:

1. Whether the product Laetrile (also known as vitamin B-17 and amygdalin) is a "new drug" within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(p)) in that it is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use in the cure, mitigation, treatment, or prevention of cancer in man ("the new drug issue").

2. Whether, if Laetrile is a "new drug" within the meaning of the act, it is exempt from the premarket approval requirements of section 505 of the act (21 U.S.C. 355) in that:

- (a) At any time before June 25, 1938, it was subject to the Food and Drugs Act of 1906, as amended, and at such time its labeling contained the same representations concerning the conditions of its use as

its present labeling ("the 1938 grandfather issue," 21 U.S.C. 321(p)(1)); or

(b) It meets each of the following conditions: (1) On October 9, 1962, it was commercially used or sold in the United States; (2) On October 9, 1962, it was generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use in the cure, mitigation, treatment, or prevention of cancer in man; (3) On October 9, 1962, it was not covered by an effective new drug application (NDA) under section 505 of the act (21 U.S.C. 355); (4) It is currently intended solely for use under conditions prescribed, recommended, or suggested in its labeling on October 9, 1962 ("the 1962 grandfather issue," Pub. L. 87-781, section 107 (c)(4)).

The February 18, 1977, notice included detailed information regarding the submission of testimony. In response to the notice, over 400 submissions totaling more than 5,500 pages were received. These submissions, representing the views of both proponents and opponents of Laetrile, came from cancer patients, consumers, experts in drug testing and cancer therapy, physicians, State governments, universities, hospitals, and interested organizations.

The District Court, in directing FDA to develop an administrative record, suggested that the agency invite the following individuals to participate in the administrative proceeding: Dr. Dean Burk, Ernst Krebs, Jr., Mike Culbert, Edward Griffin, and Mike Spencer, *Rutherford v. United States*, *supra*, 424 F.

Supp. at 108. The three individuals whose addresses could be obtained were specifically invited to give their views (R 3, 4, 5).<sup>1</sup> (Kenneth Coe, attorney for plaintiff Glen Rutherford, who had proposed that FDA be required to invite the five named individuals, could not provide the addresses for Griffin and Spencer and agreed that invitations to the three individuals whose addresses he could supply would suffice.) Mr. Griffin did receive notice of the proceeding and he participated (see R 404). Written submissions were received from Dr. Burk (R 302) and Mr. Griffin (Tr. Ex. 1) and from plaintiff Glen Rutherford (R 258).

The Bureau of Drugs, FDA, presented evidence probative of the new drug and grandfather status of Laetrile. For the purposes of the administrative proceeding, separation of functions requirements were observed between the Commissioner and persons advising him and the Bureau of Drugs and persons advising it (see 21 CFR 10.55).

The February 18, 1977 notice stated that oral argument would be held in Kansas City on May 2. A subsequent notice published in the FEDERAL REGISTER of March 25, 1977 (42 FR 16191) set forth the exact time and place: beginning at 9 a.m. on May 2 at

<sup>1</sup> Submissions to the record are referred to by the number assigned to them upon filing by the Hearing Clerk. When exhibits or attachments accompany a submission, they follow the record number of that submission, e.g., "R 12, Ex. A". References to the transcript of the oral argument are cited as "Tr. at" with the applicable page number supplied. Written submissions presented to the agency at the time of oral argument are referred to as transcript exhibits, e.g., Tr. Ex. 1.

the Radisson Muehlebach Hotel, Kansas City, MO. Dr. John Jennings, Associate Commissioner for Medical Affairs, presided over the oral argument. Approximately 40 persons filed written requests to make oral presentations; others took advantage of the opportunity to speak without the filing of such a request as time allowed. Every person who wished to participate in, and who was present at, the oral argument was given a opportunity to express his or her views. In all, 47 persons made presentations. The transcript of the oral argument has been made a part of the record of the administrative proceeding.

Individuals named by the District Court were again notified of the exact time and place of the argument (R 253-55, see also R 247). Oral presentations were made by Edward Griffin (Tr. at 11), Michael L. Culbert (Tr. at 35), Ernst T. Krebs, Jr. (Tr. at 228) and Dr. Dean Burk (Tr. at 401). In addition, plaintiff Glen L. Rutherford and his attorney, Kenneth Coe, Esq., spoke at oral argument (Tr. at 297, 442).

Written submissions presented at the time of oral argument were made part of the record and considered despite the fact that they were received at a date later than the one set forth in the February 18, 1977, notice. The record of this proceeding was, however, closed at the conclusion of the oral argument. Submissions received thereafter have been docketed with the FDA Hearing Clerk but have not been considered as part of the record. The Commissioner's opinion is based entirely upon the administrative

record and does not reflect information brought to FDA's attention subsequent to the closing of that record.

No legal memoranda were solicited by the Commissioner in this proceeding. One such memorandum was submitted by the American Cancer Society and has been made a part of this docket in the Hearing Clerk's office.

In the Commissioner's opinion, the use of Laetrile in the United States has become a genuine public health problem. Increasingly, doctors dealing with cancer patients are finding that the patients are coming to legitimate therapy too late, having delayed while trying Laetrile. It seems clear that another substantial group of persons afflicted with cancer is avoiding effective therapy altogether and using Laetrile instead. The question has become one of life and death for these patients and for others who may be convinced to use Laetrile in the future. For this reason the Commissioner has considered not only the evidence in the record addressed to the specific legal issues remanded to FDA by the courts, but also the great amount of evidence submitted by both proponents and opponents of Laetrile regarding other issues of importance to the controversy over the use of the drug. Since the Commissioner's discussion of these issues is necessarily detailed, he is setting forth, for the reader's convenience, an outline of that discussion as follows:



## I. LAETRILE

### A. DEFINITION OF CANCER

### B. COMPOSITION AND IDENTITY OF "LAETRILE"

1. Glossary.
2. What is Amygdalin?
3. What is Laetrile (with a capital L)?
4. What is laetrile (with a small l)?
5. What is Sarcocarpinase?

### C. CLAIMS FOR LAETRILE

1. Treatment (Cure or Mitigation of Cancer).
2. Analgesic (Pain Killer).
3. Prevention of Cancer.
4. Facilitation of Other Cancer Therapy.
5. Hemoglobin Index.
6. Reduction of Odor Associated with Malignancy.
7. Sickle Cell Anemia.
8. Parasitic Diseases.
9. Regulating Intestinal Flora.
10. Hypotensive Effect.

### D. THEORIES OF LAETRILE'S ACTION

## II. THE "NEW DRUG" ISSUE

### A. GENERAL RECOGNITION OF EFFECTIVENESS

1. Objective Evidence of Effectiveness.
  - (a) What are the Required Studies?
  - (b) The Need for Controlled Studies.
  - (c) The "Evidence" of Laetrile's Effectiveness.

- (i) Case Reports.
- (ii) Animal Testing of Laetrile.

### 2. Testimony of Experts.

- (a) Experts Opposed to Laetrile.
- (b) Supporters of Laetrile.

### B. GENERAL RECOGNITION OF SAFETY

1. Lack of Adequate Testing.
2. Testimony of Experts.

## III. THE "GRANDFATHER ISSUE"

### A. THE 1938 GRANDFATHER CLAUSE

### B. THE 1962 GRANDFATHER CLAUSE

1. Composition.
2. Investigational Use.
3. Conditions of Use in Labeling.
4. Lack of General Recognition of Safety in 1962.
  - (a) The Prerequisites.
    - (i) Lack of General Knowledge of Use.
    - (ii) Lack of General Knowledge of Formulation.
    - (iii) Lack of General Knowledge of Conditions of Use Suggested.
    - (iv) Lack of Safety Data in Scientific Literature.
    - (v) Lack of Showing of Safety by Adequate Testing.
  - (b) Statements by Experts.
  - (c) Lack of General Recognition of Effectiveness in 1962.

#### IV. THE POPULARITY OF LAETRILE

##### A. LAETRILE AND OTHER UNPROVEN REMEDIES

1. The History of Cancer Quackery in the United States.
2. Similarities Between Laetrile Promotion and That of Other Recent "Unproven" Cancer Remedies.
  - (a) Mantle of Science.
  - (b) Attacks on the "Establishment."
  - (c) Claimed Parallel with Scientific Pioneers.
  - (d) Reliance on Testimonials.
  - (e) Lack of Scientific Publication.
  - (f) Nonexpert Supporters.
  - (g) Simplistic Theories of Causation and Reliance on Diet.
  - (h) A Painless Cure.
  - (i) Only Proponents can Effectively Use the Drug.

##### B. WHY DO PEOPLE USE LAETRILE?

1. The Emotional Reaction to Discovery of Cancer.
2. The Role of Loved Ones.
3. Methods of Promotion of Laetrile.
4. The Sampson Survey.

##### C. THE LAETRILE TESTIMONIALS

#### V. OTHER ISSUES REGARDING LAETRILE

##### A. USE OF LAETRILE OUTSIDE THE UNITED STATES

##### B. CLAIMS THAT LAETRILE IS A VITAMIN OR FOOD

1. A Vitamin or Food May Be a Drug As Well.
2. Is Laetrile a Vitamin?

- (a) Proponents' Claims.
- (b) Vitamin Experts' Position.

##### 3. Dangers of Ingestion of "Vitamin B-17."

##### C. FREEDOM OF CHOICE

1. Balancing Freedoms.
2. The Choice Is Not Free.

##### D. ALLEGATIONS OF BIAS

##### E. LIMITING USE TO TERMINAL PATIENTS

1. Who Is Terminal.
2. Effects on Other Patients.

##### F. USE CONCURRENTLY WITH OTHER THERAPY

#### VI. CONCLUSIONS

##### I. LAETRILE

##### A. DEFINITION OF CANCER

Laetrile has been, over the years, recommended for use in the treatment of cancer. An understanding of the issues concerning the drug requires that the term "cancer" be defined. Cancer has been stated to include "\* \* \* all malignant neoplasms regardless of the tissue of origin including malignant lymphoma, Hodgkins disease, and leukemia" (R 173, Att., "Laws and Regulations Relating to the Diagnosis and Treatment of Cancer," State of California, Division 2, Chapter 7, Section 1705). For an almost identical

definition by the American Cancer Society, Inc., see R 173, Att., "American Cancer Society, Inc., Medical Affairs Department, (State) Cancer Remedy Act." A neoplasm is a new and abnormal growth such as a tumor. Malignant neoplasms are "neoplasms that are characterized by unregulated, uncontrolled, and unrestrained growth and proliferation" (R 190 at ¶ 14; R 194 at 3; R 195 at ¶ 11). It has been said that the "distinguishing feature of cancer is its ability to invade, erode and to metastasize to more or less distant parts" (R 183, Att. 7 at 15). Metastasis, in relation to cancer, means the transfer or spread of the cancer from one site to another, usually through the blood stream or the lymphatic system. In this process, cells may travel throughout the body; when they finally lodge they begin to grow as a new cancer.

There are more than 100 different entities involved in the disease known as "cancer." These many forms of clinical cancer differ materially in terms of the factors which cause them as well as in terms of populations they affect, their prognosis, and the ease with which they may be treated (Tr. at 144; cf. R 100 at ¶ 14; R 186 at ¶ 7-9). The cause of cancer is not a question addressed in this proceeding. It should be noted, however, that the record includes indications that various cancers are associated with chronic irritation (e.g., a high frequency of cancer of the groin in textile workers whose jobs required straddling a metal shaft) (R 318 at 37), with cancer-causing chemical substances called carcinogens (e.g., a high frequency of lung cancer in chimney sweepers and

coal miners probably caused by inhaling dust particles) (id.), with irradiation (id. at 38), with virus (Tr. at 223; R 318 at 38), and with hereditary effects (R 318 at 38).

Two novel theories, neither of which has gained acceptance by the scientific community, have been at various times espoused by Laetrile's proponents to explain how cancer is caused. The first of these theories is said to have been first developed by Professor John Beard of Scotland. In 1902. Professor Beard announced his "findings" that the cancer cell and the "trophoblast" cell were one and the same (R 318 at 60). Trophoblast cells are present during pregnancy and they prepare a niche in the uterine wall where the fertilized egg can nestle (R 318 at 56). According to Beard, they share several characteristics with cancer cells: Both are invasive, erosive, corrosive and can be carried through the blood stream to other parts of the body (R 318 at 57). Beard believed that trophoblast cells could be expected to develop at various places in the body from precursor cells distributed throughout the body during the embryonic stage. If the pancreas gland were functioning properly it would, in his theory, produce enzymes which destroy these trophoblast cells. If such enzymes were not produced, cancer would occur (R 318 at 58-59).

The proponents of Laetrile have more recently taken the position that cancer is a metabolic deficiency or dietary disease (cf. R 302, Ex. H at 76-77). It is claimed that cancer is a " \* \* \* systemic,



chronic, metabolic deficiency disease" (Tr. at 348) or "a chronic or metabolic disease that is not caused by some mysterious virus" (Tr. at 234). The "nutritional deficiency" theory is refuted by at least one expert (Tr. at 223).

#### B. COMPOSITION AND IDENTITY OF "LAETRILE"

Several terms, such as "Laetrile," "laetrile(s)," "amygdalin," "nitriloxide(s)," "vitamin B-17," and "Sarcarcinase" have in many instances been used interchangeably by both proponents and opponents of Laetrile. There are, however, distinctions among these terms, which must be understood in order to deal with the issues in this proceeding. The Commissioner will discuss in detail what the record indicates about the meaning of the terms "amygdalin," "Laetrile," "laetrile" and "Sarcarcinase."

##### 1. Glossary

The following glossary provides a definition or description of the above terms and others that will be used in this opinion:

**Amygdalin:** A specific chemical entity having the chemical formula:



1-mandelonitrile-beta-D-glucoside-4-beta-D-glucoside  
Chemical Index, 9th Ed. at 913.

**beta-Cyanogenic glucosides; beta-cyanophoric glucosides; beta-cyanogenetic glucosides:** Terms used interchangeably in the record. In general, they are used in the record to include compounds which can break down to yield cyanide and glucose. The terms are used to refer to amygdalin, a glucoside present in kernels or seeds of practically all fruits (see, e.g., R 302, Ex. H at 75; R 173, Att., California Administrative Code, Section 10400.1 at 16; Tr. at 272). *beta-Cyanogenic glucosides* belong to the large class of chemicals known as *beta-cyanogenic glycosides*. (See definition of glucosides and glycosides below.)

**beta-Glucosidase:** An enzyme present in plants that participates in the metabolism of glucosides. The enzyme has been identified in apricot and peach kernels and catalyzes the breakdown of amygdalin to free two molecules of glucose and a molecule of mandelonitrile. The enzyme is found only in trace amounts in animal tissues (R 173, Att., "The Vitamin Fraud in Cancer Quackery" (hereinafter "Vitamin Fraud") at 345).

**beta-Glucuronidase:** An enzyme present in animal tissues that participates in the metabolism of glucuronic acid derivatives (also called glucuronosides). The enzyme reportedly catalyzes the breakdown of "Laetrile" (1-mandelonitrile-beta-glucuronic acid) to free glucuronic acid and mandelonitrile.

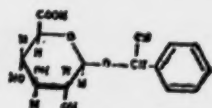
**Enzymes:** Chemical compounds (all of them proteins) produced by living organisms that serve as catalysts in metabolic reactions. The suffix "-ase" is given to most enzymes.

**Glucoside:** A term applied to any glycoside having glucose as its sugar constituent.

**Glucuronide; glucuronoside:** Terms used in the record to refer to chemical derivatives of glucuronic acid. As an example, Laetrile is identified as 1-mandelonitrile-beta-glucuronic acid" in the Merck Index 9th ed., at 702 and as "laevo-mandelonitrile-beta-glucuronoside" in the book *Control for Cancer* (R 318 at 73).

**Glycosides:** A broad term which encompasses glucosides. Not all glycosides are glucosides (cf. The Condensed Chemical Dictionary, 7th Ed. at 455).

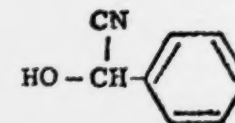
**Laetrile:** A specific chemical entity having the chemical formula:



Laetrile is 1-mandelonitrile-beta-glucuronic acid (Merck Index, 9th Ed., at 702). The name "laetrile" was perpetually assigned to this compound by Ernst T. Krebs, Jr. (R 318 at 73).

**laetrile:** A term used interchangeably with "Laetrile," "amygdalin," "nitriloside," and "vitamin B-17" (R 302, Ex. A; R 183, Att. 10c). The term is also used to include a number of compounds, in which case it may appear as "laetriles."

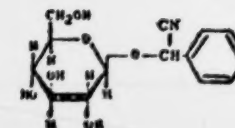
**Mandelonitrile:** A specific chemical entity having the chemical formula:



(Merck Index, 9th Ed. at 743).

**Nitriloside:** A term proposed by Ernst T. Krebs, Jr., for all cyanophorioglycosides of dietary significance (R 302, Ex. H. at 75).

**Prunasin:** A specific chemical entity having the chemical formula:



Mandelonitrile-Glucoside  
(Merck Index, 9th Ed. at 743).

**Sarcocarpinase:** The name given to an enzyme preparation developed by Dr. E. T. Krebs, Sr., and described by him in a 1933 patent application as a mixture of the following enzymes—amygdalase, prunase, oxynitrilase, catalase, peroxydase, and a proteolytic enzyme. He also suggested the presence of isomaltase and a lipase and perhaps other enzymes (R 424).

**Vitamin B-17:** Described as a group of compounds which include water-soluble, essentially nontoxic, sugary compounds found in over "800 plants" (R

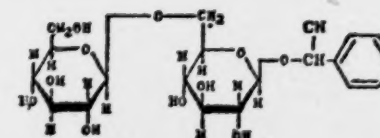
302, Ex. H at 75) used interchangeably with "nitriloxide," "Laetrile," "amygdalin," "beta-cyanogenic glucosides" and "cynophoric glucosides" (e.g., R 302, Ex. H at 75; R 302, Ex. A).

## 2. What is Amygdalin?

Amygdalin was reportedly first isolated from bitter almonds by the French chemists Robiquet and Burton-Charland in 1830 (R 173, Att., "Vitamin Fraud" at 345). The name "amygdalin" was derived from the word "amygdala", Greek for almond (R 302, Ex. L at ¶ 9). Amygdalin is a chemical compound composed of two glucose molecules and one molecule of mandelonitrile. Mandelonitrile is a chemical in which cyanide is combined with benzaldehyde (cf. R 173, Att., "Vitamin Fraud" at 345). The German chemists Liebig and Wohler observed that an enzyme preparation (later called emulsin) from bitter almonds was capable of hydrolyzing amygdalin, i.e., breaking it down into the two glucose molecules, the benzaldehyde molecule and a hydrogen cyanide molecule (id.). It was later shown that this hydrolysis occurs through the action of two enzymes (*beta*-D-glucosidase and *beta*-oxynitrilase) which are present in emulsin (id.). The *beta*-D-glucosidase hydrolyzes the *beta*-D-glucoside bond and thus frees the two glucose molecules from the mandelonitrile, *beta*-Oxynitrilase is the catalyst for the breakdown of mandelonitrile into benzaldehyde and hydrogen cyanide (id.).

Amygdalin may be extracted from apricot kernels (id.), and is present in seeds of other members of the

rose family (R 416 at ¶ 31A). The Commissioner concludes that amygdalin, a cyanogenic glucoside, is a chemical having the chemical name D-mandelonitrile-*beta*-D-glucosido-6-*beta*-D-glucoside (Merck Index, 9th Ed. at 81, compounds 630; R 183, Att. 10b). The chemical structure of amygdalin is:



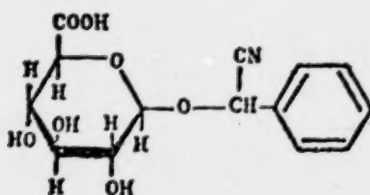
## 3. What is Laetrile (With a Capital L)?

The term "Laetrile" has been used interchangeably with "amygdalin," "laetrile," "vitamin B-17," "nitriloxides," and "*beta*-cyanogenetic glucosides" (R 173, Att., Laws and Regulations Relating to the Diagnosis and Treatment of Cancer 10400.1 at 16; R 302, Ex. A; Tr. at 405, 272, 465). It appears, however, that the term "Laetrile" (with a capital L) has been used by the drug's proponents to refer to a particular substance. There are essentially two versions of what that substance is:

(a) The term has been used to refer to a specific chemical compound which was prepared in 1952 by Ernst T. Krebs, Jr., who is said to have derived the name "Laetrile" from the compound's chemical name: laevo-mandelonitrile-*beta*-glucuronoside (R 318 at 73; see also R 262; R 183, Att. 16 at 1 and 2). This chemical is related to, but is distinctly different from, amygdalin. It is claimed that the laevo-mandelonitrile-



*beta*-glucuronoside was derived by Ernst T. Krebs, Jr., while working with the apricot extract his father had prepared and studied some 20 years earlier (R 318 at 70-73). The chemical structure of this material is depicted in several places (R 318 at 154, 157, 162) and is in agreement with the chemical name. The chemical structure of this version of Laetrile is:



(b) In a 1965 affidavit, however, Dr. Krebs, Sr., stated that the name "Laetrile" was devised in 1949 by his son, Ernst T. Krebs, Jr., for a form of amygdalin which Dr. Krebs, Sr., was producing at that time (R 183, Att. 13). As can be seen from the diagrams set out in this opinion, the chemical structure of amygdalin is different from that of Laetrile as described by Mr. Krebs, Jr.

In the second version of the identity of Laetrile, the source of the name is stated as follows: "Because this apricot preparation was 'Laevorotatory' (left-handed) to polarized light, and because Amygdalin was chemically a 'mandelonitrile,' Krebs, Jr., united the first and the last syllables to invent a name for the new cancericidal drug—LAETRILE" (R 183, Att. 7 at 24).

The confusion about the meaning of the term "Laetrile" is long-standing and may in part be the

result of a desire on the part of promoters to continue to use drugs containing amygdalin while justifying the use of the drugs by theories associated with the Laetrile of Krebs, Jr. For example, in a February 17, 1953 letter to Dr. Ian Macdonald, the Chairman of the Cancer Commission of the California Medical Association, Ernst T. Krebs, Jr., advised that he was forwarding " \* \* \* samples of the biosynthetically degraded amygdalin in which one dextrose was removed by prunasin and the resulting compound, in the presence of platinum black, was oxidized to the corresponding glucuronoside" (R 183, Att. 14). (Note: the compound thus obtained should have been 1-mandelonitrile-*beta*-glucuronoside or "Laetrile" as described by E. T. Krebs, Jr., R 318 at 73.) The Cancer Commission of the California Medical Association, in its 1953 report, stated: "Chemical analyses done independently for the Commission have identified in the product distributed as Laetrile only the presence of a natural laetrile termed amygdalin" (R 378, Att. 15 at 326).

The question of the identity of the material distributed as "Laetrile" arose again in the early 1960's when the Cancer Advisory Council of the State of California was gathering information on Laetrile in order to enforce the 1959 California law dealing with cancer quackery. In 1963 the Council reported that the California State Department of Public Health had examined different varieties of Laetrile and found that the products were markedly different in composition but did contain varying percentages of amyg-

dalín (R 183, Att. 16, App. 7 and 8). A Canadian Medical Association report published in 1965 found that the United States and Canadian versions of the drug were different—a larger percentage of the Canadian version than of the United States version was found to be made up of amygdalin (R 189; see also R 378, Att., "Supplementary Report by the Cancer Advisory Council" at 1-2).

The record reveals a number of references by Laetrile proponents which use the terms "Laetrile" and "amygdalin" interchangeably (see, e.g., Tr. at 238 and 246, and the book *Control for Cancer* (R 318)). Even some labels for the drug use the terms synonymously: one identifies the product as "Laetrile (Amygdalin) 400 mg capsules" (R 183, Att. 10a; see also R 183, Att. 10d). The National Cancer Institute, in its October 1975 "Background Statement on Laetrile" notes the fact that supporters of the drug have used the names "Laetrile" and "amygdalin" interchangeably. The report then correctly identifies amygdalin as mandelonitrile-*beta*-gentiobioside (this chemical name for amygdalin is listed in the Merck Index, 9th Ed. at 81, compound No. 630) and states that the compound actually tested in 1957, 1960, 1969, 1973, and 1975 by the National Cancer Institute was amygdalin (R 173, Att., "NCI Testing of Laetrile (Amygdalin)").

Yet it is not possible simply to conclude that the many references to Laetrile as a specific substance are a hoax on the part of Mr. Krebs, Jr., and that Laetrile as used is simply amygdalin. A number of

reports by Dr. Manuel Navarro of the Philippines stated that the Laetrile of Ernst T. Krebs, Jr., was in use (R 313 at 155, 161)), as did a report by Dr. John A. Morrone of New Jersey (R 318 at 205).

Additional confusion is added to the record by an article "Nitrilosides (Laetriles) Their Rationale and Clinical Utilization in Human Cancer (December 1962)," by Ernst T. Krebs, Jr., and Dr. N. R. Bouzi-ane, in which the authors report on their use of "non-toxic nitrilosides (Laetrile), to which the trophoblast is susceptible, on terminal cancer cases for two years in Canada \* \* \*" (R 318 at 187). While the article refers to "cyanophoric glucosides and cyanophoric glucuronosides" (id. at 189), the authors do not identify the "Laetrile" they had been using and about which they were reporting. The authors cite a chemical compound in their discussion (id. at 190) that is not amygdalin nor is it "Laetrile" as described and named by Ernst T. Krebs, Jr. (id. at 73).

While the prevailing confusion over the true identity of material called "Laetrile" would be a severe drawback to anyone seeking to show through testing that Laetrile was safe and effective, this lack of uniformity has been adopted by Laetrile proponents as a means of discounting data showing the drug to be ineffective and thus unsafe. An example is found in the statement by Ernst T. Krebs, Jr., that "The \* \* \* single negative report on Laetrile, which is based upon the observations of unidentified investigators in unidentified institutions administering a purported Laetrile not obtained from the only source of the

material, is to be found in California Medicine, 78:320 (1953)" (emphasis added) (R 318 at 251). It should be recalled that at least some of the material supplied to the California Cancer Commission was sent by Ernst T. Krebs, Jr., himself (R 183, Att. 14). In May of 1971, Mr. McNaughton of the pro-Laetrile McNaughton Foundation, in a meeting with FDA's Ad Hoc Committee of Oncology Experts, stated that data obtained prior to 1968 are frequently not valid because of the variability of Laetrile formulations (R 173, Att. "Report of the Ad Hoc Committee of Oncology Consultants" at 1). See also statement of Robert Bradford, President of the Committee for Freedom of Choice in Cancer Therapy, Inc.: "As an aside, an important aspect of animal tests, and indeed, of human tests has been from time to time the availability of amygdalin which did not meet the specified identification criteria, that is, for its use. Tests with defective materials, as Sloan-Kettering found out, will not be efficacious. Defective material likewise will not be effective in humans" (Bradford, Tr. at 350).

In its 1971 report to FDA, the Ad Hoc Committee of Oncology Consultants agreed that uncertainty about the identity of the drug tested makes the test results obtained questionable. The Committee stated that because of the variability in composition of early preparations, doubt was cast on the bulk of the 1970 McNaughton Foundation Notice of Claimed Investigational Exemption for a New Drug (IND) for Laetrile, which was based almost exclusively on such

early material (R 173, "Report of the Ad Hoc Committee of Oncology Consultants" at 1). The Committee further suggested that any protocol for study contain a full description of the drug (formulation, stability etc.) (id. at 4).

There is, quite simply, no one answer to the question "What is Laetrile?". In the glossary to this opinion, the chemical composition of Laetrile is considered to be that described by Ernst T. Krebs, Jr. Yet if some other substance is being used to treat cancer patients, testing of that "Laetrile" would be of no relevance.

Because different persons have used the terms "Laetrile" and "amygdalin" to mean different substances, uniformity of definition will not be possible in discussing the evidence in the record. For this reason, the Commissioner will not, in quoting or citing parts of the administrative record, attempt to define or to determine the identity of the material under discussion but will simply use the term as it appears in that portion of the record. Attempts to identify the material referred to will be made only when necessary for a rational resolution of an issue, e.g., a reference to Sarcarcinase as amygdalin or as Laetrile will not be accepted blindly.

#### 4. *What is laetrile (With a Small l)?*

As noted in the glossary, the term "laetrile" (with a small l) has been used interchangeably with or synonymously for: nitriloside, Laetrile, vitamin B-17, and amygdalin (e.g., R 302, Ex. A; R 183, Att. 10c;



R 378, Att. 6). The term has, however, also been used to describe a class or group of compounds. For example, amygdalin and prunasin are described as "two common Laetriles" (R 173, Att., "Vitamin Fraud" at 345). It has been stated that: "The term LAETRILE is used to designate the laevorotatory containing glucosides in general and the corresponding glucuronoside in particular. The former are found in plants whereas the latter are synthetic" (*italics in original*) (R 318 at 155). (See also, R 318, at 240 ¶ 9 which defines natural laetriles as *betacyanogenetic glucosides and glucuronosides.*) The Commissioner concludes that the term "laetrile" is an imprecise term and that it does not imply a specific chemical compound. The term is, rather, a broad or generic term for a group of compounds of unknown number.

##### 5. *What is Sarcarcinase?*

Dr. Ernst T. Krebs, Sr., claims to have developed a product called "Sarcarcinase" in 1926 (R 183, Att. 13). "Sarcarcinase" is stated to be a registered trademark in the United States and 10 other countries (with registrations dating from March 1933 to January 1934) (see R 260; R 259). The process for preparing the product is stated to be patented in 15 countries including the United States (see R. 260). It is also reported that Sarcarcinase was used in Japan in 1934 and in Czechoslovakia in 1935 (R 259). Other references in the same timespan refer to an "enzyme preparation" or "enzyme injection"

used within the United States as well as several foreign countries (*id.*).

Ernst T. Krebs, Jr., stated at oral argument that as early as 1932 his father "\* \* \* observed the use of amygdalin, or laetrile; made it available across the country and abroad under the term 'Sarcarcinase' to physicians, to researchers" (Tr. at 233). He also stated, "\* \* \* the first amygdalin was used—1932—it was labeled as 'Sarcarcinase'" (Tr. at 246). Sarcarcinase was not, however, amygdalin nor did it contain amygdalin in any quantity. Rather, in the words of Dr. Krebs, Sr.'s 1933 patent application, Sarcarcinase was "an enzyme for treatment of malignant growths." The patent application actually describes the product as "an enzyme complex" containing "amygdalase, prunase, oxynitrilase, catalase, peroxydase and proteolytic enzyme" plus a suggestion of "isomaltase and lipase with possibly others" (Patent application attached to R 424 and to R 259).

Amygdalin is not an enzyme. As will be discussed in more detail below, enzymes are chemicals which catalyze the breakdown of other chemicals and which are often named by attaching the ending "-ase" to the chemical which they attack. Thus, "amygdalase," stated by Dr. Krebs, Sr., to be part of his enzyme complex, may have been meant to describe an enzyme which would break down amygdalin.

It has been argued that Sarcarcinase contained some quantity of amygdalin (R 183, Att. 13, and Att. 7 at 23). An expert chemist has stated, however, that much or all of the small amounts of amyg-

dalín in the apricot kernels used in making Sarcarcinase would be destroyed by enzyme action when the kernels are ground up and that only a small fraction of any that remained would survive the rest of the process (R 424). It should be noted that, even if there were any amygdalin in Sarcarcinase, that would not make that drug equivalent to a drug made up of amygdalin either totally or in greater proportions either in a scientific sense or in a legal sense.

There is some indication that Dr. Krebs, Sr., had abandoned Sarcarcinase even at the time when the patent applications were being obtained. One submission by a Laetrile proponent states that Dr. Krebs, Sr., " \* \* \* resigned himself to the fact that there was no sense continuing this particular research to identify the toxic element or elements in the apricot extract he prepared (sometime after 1926) until he acquired the additional knowledge necessary to understand the mysteries that were occurring in his test tubes. He put his extract aside and returned his books" (R 318 at 42). Krebs himself states that in 1936 he developed a new product, whose "active principle" was amygdalin of 66 percent purity (R 183, Att. 13). (The inactive ingredients of this preparation are not identified.) It is not clear whether it is Sarcarcinase or this new product about which Krebs, Sr., speaks when he states that his "apricot extract" was "so toxic that he and colleagues who were experimenting with him were reluctant to continue its use, except in dire circumstances" (R 183, Att. 7 at 23). Its was apparently these toxicity problems that led

Krebs, Jr., to seek to improve his father's work (id.). Since "Laetrile" was not developed until 1952 by Krebs, Jr., any statement that "Laetrile" was sold as Sarcarcinase in the 1930's is patently erroneous.

#### C. CLAIMS FOR LAETRILE

Laetrile (or amygdalin) has been recommended over the years primarily for use in the treatment and, more recently, "control" of cancer. The claims appear to vary in relation to the sophistication of the intended audience. Thus in the 1962 new drug application (NDA) for Laetrile submitted by Ernst T. Krebs, Jr., to FDA, the drug was claimed to be a palliative (i.e., a drug that mitigates the symptoms of a disease without curing it) to be used with other recognized therapies (R 201, Ex. B at 102). By contrast, in a pamphlet in use in 1965, apparently addressed in part to prospective patients, it is stated that "Laetrile does not palliate, it acts chemically to kill the cancer cell selectively \* \* \*," and use of other cancer therapies concurrently is discouraged (R 201, Ex. C., # III). The following claims have been made for Laetrile (amygdalin):

##### 1. *Treatment (Cure or Mitigation) of Cancer*

The pamphlet discussed above and others obtained from Dr. Krebs, Sr., by FDA investigators at the same time recommended Laetrile for treatment of cancer (see, generally, R 201, Ex. C). Dr. Krebs, Sr., in a pamphlet entitled "The Treatment of Breast

Cancer with Laetrile by Iontophoresis" promotes the drug for treatment of a number of cancers (R 183, Att. 7 at 26-27 and 30).

A label for 400 mg capsules of "Laetrile (Amygdalin)" claims that the "nontoxic cyanide glucoside is used for specific treatment of cancer by physicians or under directions of a physician" (R 173, Att. 102). Amygdalin has been promoted (as an ingredient of "Bitter Food Tablets") for the cure, mitigation, and treatment of cancer in man (R 173, Att., *United States v. Spectro Foods*, Civ. No. 76-101 (D.N.J., Jan. 28, 1976) Findings 16 through 23).

As noted above, some claims are limited to palliation. (See, e.g., R 216 at 348; R 318 at 175; Tr. at 238.) Recently, Laetrile has been touted as a "control" for cancer. Proponents of Laetrile making this claim assert that no "cure" for cancer exists (see Tr. at 303). Control for Cancer is also the title of a paperback book on Laetrile (R 318). It is not entirely clear from the record whether "control" means palliation. Laetrile therapy is said to be responsible for increased appetite and weight gain and an increased "sense of well-being" among treated cancer patients (R 318 at 158 and 165).

## 2. Analgesic (Pain Killer)

An information booklet for physicians about amygdalin makes the claim that the product is a nontoxic analgesic that is highly effective in relieving the pain of terminal cancer (R 183, Att. 10b). The booklet

claims that the oral route is the most convenient route of administration for both patient and physician.

NOTE.—The Commissioner points out that both proponents and opponents have warned against oral use of amygdalin or Laetrile.

See R 318 at 167: "\* \* \* it (Laetrile) should never be given by mouth because the HCl (of the stomach) is capable of hydrolyzing the Laetrile"; see also R 318 at 158. Compare R 173, Att., Interview with Robert C. Eyerly, American Cancer Society: "Taken orally, it (Amygdalin) is decomposed in the intestinal tract by *beta*-glucosidase into highly lethal hydrogen cyanide." "Orally it (Laetrile) is extremely toxic due to the release of hydrogen cyanide on contact with the hydrochloric acid of the gastric juice (R 318 at 205).

A label for "The Original Laetrile" claims that the product "relieves pain due to malignancy" (R 183, Att. 9). For another claim that Laetrile reduces cancer-connected pain, see Tr. at 44. It has also been asserted that the hydrogen cyanide and benzaldehyde liberated by hydrolysis of Laetrile are potent analgesics (R 318 at 164).

## 3. Prevention of Cancer

With the advent of their theory that cancer is a deficiency disease and that that deficiency can be overcome by their product, either characterized as a pro-vitamin for vitamin B-12 (R 201, Ex. C, No. IV), or as new vitamin B-17 (see R 183, Att. 10c), pro-



ponents of Laetrile have promoted it as a preventative for cancer (see the above references and R 198, Ex. 2 (transcript of the film *World Without Cancer*); cf. Tr. at 465). (See also R 173, Att., *United States v. Spectro Foods*, supra, Findings 16 through 23.) While proving that Laetrile (or amygdalin) did not prevent cancer would be extremely difficult, the record does contain evidence that at least one person taking it as a preventative did contract cancer (Tr. at 120).

#### 4. *Facilitation of Other Cancer Therapy*

While, as noted above, some labeling recommends against use of other cancer therapies with Laetrile, it has been stated that “\* \* \* if you combine toxic chemotherapy with Laetrile, you can give very high doses of toxic chemotherapy with no side effects, physical and no effects on the blood. That is, you don’t get neutropenia (leukopenia?) and you don’t get chromositopenia (chromocytopenia?)” (Tr. at 480).

#### 5. *Hemoglobin Index*

One set of labeling for “Laetrile (Amygdalin),” which appears at two points in the record, recommends the product “for raising hemoglobin index and red count \* \* \*” (R 183, Att. 9; R 201, Ex. C. No. 1).

#### 6. *Reduction of Odor Associated with Malignancy*

It is also claimed that topical application of Laetrile relieves fetor (odor) resulting from the second-

ary infection of ulcerated carcinoma and that parenteral administration takes care of fetor associated with internal cancers. This action is ascribed to the “antiseptic” properties of HCN and benzaldehyde, which is converted by the cells to benzoic acid (R 318 at 158 and 165).

#### 7. *Sickle Cell Anemia*

It is theorized that nitriloside (Laetrile) might be of value in the treatment of sickle cell anemia because of the release of cyanide and the subsequent formation of thiocyanates (R 217, article by R. G. Houston). (See also Tr. at 465.) This claim is reportedly refuted by experts in sickle cell hemoglobin (R 416 at 23).

#### 8. *Parasitic Diseases*

The Houston article also references a report by Navarro and others of the clinical control of schistosomiasis (a snail-borne infection) with nitriloside (Laetrile) (R 217, Houston article at 58). The possibility of using Laetrile to treat parasitic diseases such as schistosomiasis or malaria is discussed in the book *Control for Cancer* but there are no reports of actual use in the book (R 318 at 111-12).

#### 9. *Regulating Intestinal Flora*

It has also been suggested that amygdalin has some utility in regulating intestinal flora (Tr. at 476).

### 10. Hypotensive Effect

It has also been claimed that use of Laetrile causes a hypotensive effect (i.e., it reduces blood pressure), at least in cancer patients (R 318 at 165; cf. Tr. at 465).

In addition to these claims by Laetrile proponents (developers, distributors, and promoters), numerous comments from interested citizens contained references to or claims for its therapeutic effects as a cancer cure or as a preventative. There are also references to relief, attributed to Laetrile, from other ailments unrelated to cancer, e.g., arthritis (R 391).

#### D. THEORIES OF LAETRILE'S ACTION

A thorough understanding of the manner in which a compound achieves its therapeutic or beneficial effects is highly desirable. A cancer drug which had been shown to be safe and effective would not, however, be denied marketing approval simply because its action could not be explained. Experience has shown that a good theory to explain or predict the action of a chemical in the body, does not assure success; neither does a weak theory, or even what turns out to be a totally incorrect theory, mean certain failure.

Some cancer patients may be turning to Laetrile in the mistaken belief that its use is supported by a respectable—even if not widely accepted—scientific theory. (Unproven remedies throughout the years have benefited from the use of the type of “scientific”

theories associated with Laetrile (see, generally, R 413.) The Commissioner finds from the record that the theories advanced for Laetrile's supposed action are based on false or questionable assumptions. An understanding of these theories, furthermore, points up important differences between the “Laetrile” whose use is “justified” by the theories of Krebs, Jr., and the amygdalin-containing products actually being used.

Since a large part of the Laetrile theory of action deals with enzymes, the Commissioner believes that a few brief introductory comments about enzymes would be useful. Enzymes are protein molecules manufactured in the cells of the body which help the cells perform chemical reactions involving other compounds. As an example, trypsin, a common enzyme, aids in the metabolism of proteins in food by breaking these large molecules into smaller, easier-to-handle pieces. Enzymes generally are very specific in the types of chemicals they will attack. Frequently, the name of an enzyme is derived from the compounds that enzyme will break down. The ending “-ase” is often used to indicate an enzyme.

The chemical “*beta*-glucosidase” appears frequently in the Laetrile record. The name of this chemical indicates that it is an enzyme (-ase) and, furthermore, the name indicates that it attacks glucose-containing compounds (glucosides) from which it will liberate glucose molecules. As an example, *beta*-glucosidase liberates two molecules of glucose from

amygdalin. If the chemical compound does not contain glucose molecules, *beta*-glucosidase will not attack it. In a similar vein, *beta*-glucosidase will attack chemical compounds that contain glucuronic acid. (These chemical compounds are called "glucuronides" or "glucuronosides" or "glucuronic acid derivatives.")

The original theory of Ernst T. Krebs, Jr., for Laetrile's action involved two enzymes, rhodanese and *beta*-glucosidase (R 318 at 72). Krebs claimed that normal cells produced these two enzymes, while cancer cells were deficient in rhodanese. In cancerous areas, the theory continues, the *beta*-glucosidase accumulates in great quantities (R 318 at 72).

According to the theory, when Laetrile comes into contact with the cancerous areas it is hydrolyzed by the enzyme *beta*-glucosidase to liberate cyanide and benzaldehyde. In normal cells, the enzyme rhodanese converts the liberated cyanide to the less toxic thiocyanate. Cancer cells, lacking rhodanese, are said to be killed by the liberated cyanide when it reacts with cellular components. Rhodanese from normal cells cannot protect cancer cells because, it is claimed, cancer cells produce chorionic gonadotropic hormone that effectively blocks the action of rhodanese (R 318 at 153). In later versions of the theory, the benzaldehyde is also considered to be responsible for killing the cancer cells, either alone or in concert with the cyanide. According to this theory, benzaldehyde is normally converted by a cell to benzoic acid by oxidation. Cancer cells are said to oxidize the benzaldehyde at a slower rate than normal cells, making it

toxic to cancer cells and nontoxic to normal cells. (See Krebs, Jr., "The Nitrilosides (Vitamin B-17)—Their Nature, Occurrence and Metabolic Significance (Antineoplastic Vitamin B-17)" (R 183, Att. 10c at 80).)<sup>2</sup>

In fact, it has been reported that only traces of *beta*-glucosidases have been found in animal tissues and even less in experimental tumors than in such organs as liver and spleen (R 173, Att., "Vitamin Fraud" at 345). Apparently for this reason, Krebs, Jr., at one time modified his theory. In the modified version it is *beta*-glucuronidase rather than *beta*-glucosidase which is abundant in cancerous areas. This change is reflected in a 1955 pamphlet co-authored by Dr. Krebs, Sr., and Dr. Arthur T. Harris, in which it is stated: "As soon as the Laetrile *beta*-glucuronidase, which bathed the cancer cell, because of its affinity for sugar split the glucoside (or sugar radical) from the Laetrile molecule" (R 183, Att. 7 at 24). (See also R 318 at 151-53.)

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<sup>2</sup> In his 1933 patent application for Sarcocarpinase, Dr. Ernst T. Krebs, Sr., discussed his own theory of cancer, apparently now abandoned by Laetrile proponents. He perceived a malignant protein ("\* \* \* a so-called abnormal glucosido-protein \* \* \*") in cancer cells and explained why his enzyme extract, prepared from apricot kernels, should be effective against those cells (R 424). He believed that the enzyme would break up the abnormal gluco-protein and thus be an effective treatment against cancer (R 318 at 40-41). While it is claimed that some positive effects were observed in cancers in mice, the extract proved to be toxic and Dr. Krebs, Sr., discontinued working on the extract (id. at 42).



The change in theory is important. *beta*-Glucuronidase hydrolyzes (breaks down) *beta*-glucuronosides (or "*beta*-glucuronic acids" or "*beta*-glucuronides") but does not hydrolyze *beta*-glucosides (R 318, Att. 16 at 24). Thus, *beta*-glucuronidase will hydrolyze "Laetrile" of the formulation devised by Krebs, Jr. (i.e., laevo-mandelonitrile-*beta*-glucuronoside), but it will not hydrolyze amygdalin (D-mandelonitrile-*beta*-D-glucosido-6-*beta*-D-glucoside) or other "nitrolo-sides" found in nature. What this means is that amygdalin, which has been sold as "Laetrile," would not be hydrolyzed by the body to liberate cyanide (R 183, Att. 16 at 41).

Recognition of this fact apparently led Krebs, Jr., to formulate his version of Laetrile in the first place. He is reported to have stated in a manuscript that "the natural laetriles have been abandoned for the more specific synthetic laetrile tailored as specific glucuronosidic substrates for the tumor *beta*-glucuronidase" (R 183, Att. 16 at 14).

The specificity of *beta*-glucuronidase for glucuronides (or glucuronosides) and its lack of activity against glucosides (such as amygdalin) is rigorously addressed in the record:

Numerous glucuronides are hydrolyzed by *beta*-glucuronidase. \* \* \* Methyl-alpha-D-glucuronide and alpha-and beta-methyl-D-glucosides are not split by the enzyme.

Further checking of this important point is consistent with the idea that the enzyme in question (*beta*-glucuronidase) not hydrolyze the *beta*-

glucosides, which are the only Laetriles actually utilized by the Krebs' for human treatment (R 183, Att. 16 at 24).

(It should be remembered that the Cancer Commission of the California Medical Association had determined that the material labeled "Laetrile" was in fact amygdalin—a glucoside and not a glucuronoside (R 183, Att. 15 at 326.)

The conclusion seems justified that the presence of the terminal carboxyl group on position 6 appears to be the important factor in determining a specificity which is markedly different from that of B. Glucosidase \* \* \* (R 183, Att. 16 at 25).

(The Commissioner points out that amygdalin has two glucose molecules but does not have a carboxyl group. Laetrile, as reportedly prepared, described, and named by Ernst T. Krebs, Jr., in the late 1940's or early 1950's (R 318 at 73) does have a carboxyl group on position 6 (the glucuronic acid portion of the molecule).)

Dr. Krebs, Sr., in his 1955 pamphlet on Laetrile appears to recognize that "animal *beta*-glucuronidase" and *beta*-glucosidase are different substances. (He characterizes the latter as a "prepared enzyme.") He does claim that the two enzymes react with Laetrile in the same manner (R 183, Att. 7 at 24).

There is some indication that Ernst Krebs, Jr., in later years abandoned his attempt to develop a Laetrile that could be broken down by *beta*-glucuronidase and began treating *beta*-glucuronidase and *beta*-glu-

cosidase as equivalent. In a 1962 letter, Krebs, Jr., seems to refer to the former as an example of the latter: "beta glucosidases (e.g., beta glucuronidase)" (R 183, Att. 16, App. 12 at 2) and seeks, in describing an experiment with water fleas he had designed, to extrapolate results obtained with *beta*-glucosidase to results with *beta*-glucuronidase he feels is found in malignant lesions (id. at 4). (See also Krebs' 1970 article "The Nitrilosides (Vitamin B-17)—Their Nature, Occurrence and Metabolic Significance (Anti-neoplastic Vitamin B-17)" in which he again equates *beta*-glucosidase with *beta*-glucuronidase (R 183, Att. 10c at 82).)

Three other problems with this theory are quickly identifiable: (1) there is evidence that *beta*-glucuronidase is not particularly abundant in malignant tissues. The record shows that "\* \* \* *beta*-glucuronidase is found in all tissues of the animal body and in particularly high concentrations in spleen, liver, and endocrine organs, as well as in plasma and in tumors arising from estrogen-influenced tissues. Per gram of tissue, the spleen and liver have a higher concentration of *beta*-glucuronidase than do most tumors," (R 183, Att. 16 at 15 and App. 14). It is further stated, "Such a statement as '\* \* \* the malignant cell \* \* \* is virtually an island surrounded by a sea of *beta*-glucuronidase' is sheer nonsense" (R 183, Att. 16 at 15 and App. 14).

(2) There is no evidence that cancer cells are deficient in the enzyme rhodanese. In reviewing the record, the Commissioner has not found any support for

the bald assertion by the Krebs and other Laetrile proponents that cancer cells are deficient in the production of a hydrogen cyanide-inactivating enzyme called rhodanese. If there is any scientific support for that assertion, it is indeed strange that it has never been cited by the Krebs' or otherwise brought to the attention of the scientific community. The record shows, in fact, that: "There is no evidence of pronounced differential between the rhodanese content of comparable normal and cancerous tissue" (R 378, Att. 9 at 346).

(3) The complete breakdown of Laetrile into cyanide may require an enzyme not found in animal tissues. Hydrolysis of Laetrile by *beta*-glucuronidase (and hydrolysis of amygdalin by *beta*-glucosidase) only represents the first step in breaking down the molecules to release hydrogen cyanide and benzaldehyde (which are supposed to kill the cancer cell). The first reaction in each case would yield mandelonitrile plus (for Laetrile) glucuronic acid or (for amygdalin) glucose. Mandelonitrile must then be hydrolyzed or broken down to yield hydrogen cyanide and benzaldehyde (R 416 at ¶ 8).

Enzymes present in apricot kernels (specifically oxynitrilase) will hydrolyze mandelonitrile to cyanide and benzaldehyde, but this enzyme is not reported to exist in animal tissues (R 399 at ¶ 7B). Nor does the record show that any other enzyme capable of breaking down the mandelonitrile exists in animal tissues (or in malignant lesions). Thus, if Laetrile were injected into the blood stream and did go to the

malignant lesion, even if it were broken down into mandelonitrile and gulcuonic acid, it might never be further broken down to yield hydrogen cyanide and the supposed action of that substance in killing the cancer cell would never take place.

At one time, Ernst T. Krebs, Jr., apparently attempted to deal with some of these problems by separating out the elements of the apricot extract his father had prepared. The fact that both *beta*-glucosidase and oxynitrilase are present in apricot pits and thus in the extract provides the potential for the whole breakdown process to occur in the apricot extract itself at the time when it is prepared. Krebs, Jr., sought to prevent this from happening (and perhaps sought to reduce toxicity) by separating amygdalin from "emulsin" by purifying the apricot extract. Emulsin contains, among other things, *beta*-glucosidase and *beta*-oxynitrilase (R 173, Att., "Vitamin Fraud" at 345).

Ernst T. Krebs, Jr., reportedly separated amygdalin from emulsin in 1952 and "\* \* \* advised their administration separately in order to avoid the premature trigger-off of HCN (hydrogen cyanide) from the chemical breakdown in the somatic (or normal) tissue \* \* \*" (R 183, Att. 7 at 23). It is further stated that by injecting the cyanogenetic glucoside (amygdalin) followed 15 minutes later by the enzyme *beta*-glucosidase a "high degree of safety" as well as cancerolytic effect was obtained (id. at 23-24).

If the *beta*-glucosidase preparation reached the same area of the body that the amygdalin had

reached, its presence would lead to the breakdown of amygdalin to release mandelonitrile (see R 416 at ¶ 18; R 183, Att. 7 at 31). While Ernst T. Krebs, Jr., apparently recommended that the second injection be of emulsin (R 183, Att. 7 at 23), Dr. Krebs, Sr., states that his second injection would consist only of the enzyme *beta*-glucosidase (id. at 24). If the second injection did contain emulsin, the presence of the oxynitrilase in that complex might in fact lead, assuming the emulsin caught up with the amygdalin in the body, to breakdown of the mandelonitrile to release hydrogen cyanide (and benzaldehyde). However, there is little reason to believe that this release of cyanide would occur only in or near tumor cells. (In the same article in which Ernst T. Krebs, Sr., explained the process of injecting the *beta*-glucosidase, he stated his understanding that it was the *beta*-glucuronidase" which bathed the cancer cell" that acted to break down the amygdalin (id. at 25).) It should be noted that, since the time of the 1955 pamphlet, no evidence has appeared, at least in this record, that two injections, one containing *beta*-glucosidase, are being used in Laetrile therapy.

In light of the above, one must be concerned that products are being used that contain not only amygdalin but emulsin. As the Krebs themselves recognized, unless emulsin is separated from amygdalin (both of which exist in the apricot extract), there may occur the premature trigger-off of HCN (hydrogen cyanide) from the chemical breakdown in the somatic (or normal) tissue (R 183, Att. 7 at 23).



It is this type of cyanide poisoning which has occurred from ingestion of Laetrile and from eating apricot kernels. (See R 378, California Morbidity, Nov. 14, 1975, No. 45.)

It is thus clear that the theory propounded by the promoters of Laetrile is based on faulty and unproven assumptions. The invention of Laetrile as described by Krebs, Jr., and his suggestion that an injection of amygdalin be followed by an injection of emulsin were two different ways to deal with the fact that enzyme *beta*-glucosidase does not exist in human tissues. What is perhaps most important about the proffered theoretical justification for Laetrile's action is that, even if they were accepted, they would not justify the administration of amygdalin alone.

## II. THE "NEW DRUG" ISSUE

The Commissioner will now address the first of the two issues remanded to the agency: Whether Laetrile is a "new drug" within the meaning of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 et seq. (hereinafter the act). Based upon a careful review of the administrative record, as detailed below, the Commissioner finds that Laetrile is not generally recognized by qualified experts as a safe and effective cancer drug. Accordingly, the Commissioner concludes as a matter of law that Laetrile is a new drug and thus subject to the premarket approval requirements of the act.

The term "new drug" is defined by section 201(p) (1) of the act (21 U.S.C. 321(p)(1)) as follows:

Any drug \* \* \* the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof \* \* \*.

Although the act defines "new drug", it does not contain a definition of "generally recognized as safe and effective."

In 1973, the Supreme Court, in a series of four cases (*Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609 (1973); *Ciba Corp. v. Weinberger*, 412 U.S. 640 (1973); *Weinberger v. Bentex Pharmaceuticals, Inc.*, 412 U.S. 645 (1973); *USV Pharmaceutical Corp. v. Weinberger*, 412 U.S. 655 (1973)) involving the procedures adopted and utilized by FDA to regulate new drugs pursuant to the Drug Amendments of 1962 (76 Stat. 780), established the legal principles that are applicable and controlling here. In *Hynson*, the Court discussed "general recognition" as it pertains to the effectiveness of a drug as follows:

The thrust of § 201(p) is both qualitative and quantitative. The Act, however, nowhere defines what constitutes "general recognition" among experts. \* \* \* We agree with FDA, however, that the statutory scheme and overriding purpose of the 1962 amendments compel the conclusion that the hurdle of "general recognition" of

effectiveness requires at least "substantial evidence" of effectiveness for approval of an NDA. In the absence of any evidence of adequate and well-controlled investigation supporting the efficacy of (a drug), a fortiori (that drug) would be a "new drug" subject to the provisions of the Act. 412 U.S. at 629-30.

\* \* \* \* \*

We accordingly have concluded that a drug can be "generally recognized" by experts as effective for intended use within the meaning of the Act only when that expert consensus is founded upon "substantial evidence" as defined in § 505(d). 412 U.S. at 632.

The term "substantial evidence" is defined in the last sentence of section 505(d), 21 U.S.C. 355(d), as:

evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

In *Bentex*, based upon its discussion of the term "general recognition" in *Hynson*, the Court concluded:

Whether a particular drug is a "new drug" depends in part on the expert knowledge and expe-

rience of scientists based on controlled clinical experimentation and backed by substantial support in scientific literature. 412 U.S. at 652.

It accordingly held that "the reach of scientific inquiry under both section 505(d) and under section 201(p) is precisely the same" (*id.*).<sup>3</sup>

The requirements that a drug have not only controlled clinical investigations but also publication of the studies concerning it in the scientific literature are designed to assure that the community of qualified experts in general is aware of the data concerning the drug. Thus, one could not obtain general recognition just by doing the required studies without publishing them in the scientific literature, making them available to other scientists. (Studies submitted to scientific publications must undergo peer review before they are published. A study published in a scientific journal is thus more likely to form a basis for expert recognition than is one published by the lay press.) A practical effect of the statutory system, as the Supreme Court acknowledged in *Hynson*, *supra*, is that drugs will have accumulated for themselves sufficient scientific evidence to justify approval of an NDA "long before they are in a position

<sup>3</sup> Section 505(d) of the act (21 U.S.C. 355(d)) sets forth the standards applicable to obtain marketing approval of a new drug. With respect to reports of investigations which are required to be submitted concerning the safety of a drug, the act provides that such reports must include "adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof".

to drop out of active regulation by ceasing to be a 'new drug' " (412 U.S. at 631).

Under the Supreme Court's authoritative interpretation of the act, therefore, general recognition of the safety and effectiveness of Laetrile depends upon two criteria: (1) Controlled clinical investigations conducted by qualified experts establishing the safety and effectiveness of the drug and published in the scientific literature, and (2) expert consensus, based upon that evidence, that the drug is safe and effective. Both requirements must be met in order for Laetrile to escape the need for premarket approval under the act; however, a finding of a failure to meet either set of requirements is sufficient to classify the drug as a new drug.

With respect to the first criterion, the safety of Laetrile must be established by adequate tests by all methods reasonably applicable (see 21 U.S.C. 355 (d); 21 CFR 314.111(a)(1)). In addition, the effectiveness of Laetrile must be established by "substantial evidence," which the statute (21 U.S.C. 355(d)) defines as evidence consisting of adequate and well-controlled clinical investigations. (Clinical investigations are studies involving human beings as test subjects.) The requirements for an adequate and well-controlled clinical investigation are set forth in 21 CFR 314.111(a)(5) (see discussion below). Both types of testing must be available to the community of experts in the evaluation of drug safety and effectiveness by means of publication in the scientific literature.

For satisfaction of the second criterion, a showing must be made of recognition among the qualified experts which is "general." It has been held that a genuine difference of opinion among experts on the question of general recognition is sufficient to show that such recognition of a drug's safety does not exist (see *United States v. An Article of Drug, Etc.*, 294 F. Supp. 1307, 1311 (N.D. Ga. 1968) aff'd 415 F. 2d 390 (5th Cir. 1969); *United States v. 354 Bulk Cartons, Etc.*, 178 F. Supp. 847, 853 (D.N.J. 1959); *Merritt Corp. v. Folsom*, 165 F. Supp. 418, 421 (D. D.C. 1958)). This interpretation of "general recognition" has been criticized as requiring "unanimous" recognition (see *United States v. 7 Cartons, More or Less, Etc.*, 293 F. Supp. 660, 662-63 (S.D. Ill. 1968) aff'd 424 F.2d 1364 (7th Cir. 1970)). For purposes of completeness, the Commissioner in his opinion will consider "general recognition" to require, as the 7 Cartons Court suggested, recognition "extensively, though not universally; most frequently, but not without exception" (id.).

#### A. GENERAL RECOGNITION OF EFFECTIVENESS

##### 1. Objective Evidence of Effectiveness

The Courts thus have determined that, as a matter of law, no "general recognition" of a drug's effectiveness can exist absent adequate and well-controlled clinical investigations and substantial support in the scientific literature. There are no clinical investigations of Laetrile's effectiveness, published or other-



wise, which are even arguably adequate and well-controlled. (See, e.g., R 185 at ¶ 19; R 186 at ¶ 12; R 390 at ¶ 19). For this reason, Laetrile cannot escape “new drug” status as “generally recognized” as safe and effective. It is thus a new drug without an approved new drug application whose sale or distribution, where interstate commerce is involved, is illegal.

There is, however, an apparent public lack of understanding of what the required studies consist of and why they are required. The Commissioner will thus include in this opinion a discussion of what adequate and well-controlled studies are and why they are needed. He will then discuss the deficient “evidence” of effectiveness submitted by Laetrile’s proponents.

(a). *What Are the Required Studies.* “(A)adequate and well-controlled clinical investigations,” as those terms are used in the act (21 U.S.C. 355(d)) are defined in detail by regulation (21 CFR 314.111 (a)(5)(ii)). These regulations, discussed with approval by the Supreme Court in *Weinberger v. Hynson, Westcott & Dunning, Inc.*, *supra*, 412 U.S. at 617-19, were upheld in *Upjohn v. Finch*, 422 F.2d 944 (6th Cir. 1970) and *Pharmaceutical Manufacturers Ass’n v. Richardson*, 318 F. Supp. 301 (D. Del. 1970). Simply stated, such investigations are designed to determine whether an improvement noted after administration of a drug is in response to the drug or whether it is caused by some other factor.

To do this, patients as nearly identical in their disease state as possible are divided into groups and treated, insofar as possible, exactly the same in all respects except one: One group receives the test drug; the other receives a placebo (a substance that looks just like the test drug but is not a drug). Since a patient might feel better through knowledge of receiving the test drug, and since the investigator might subconsciously record better results because of the knowledge that he or she were administering the test drug, the experiment is “double-blind”: Neither the patient nor the investigator knows until after the experiment which patient is getting the test drug and which the placebo. If, at the end of the investigation, the patients receiving the drug did better than those not receiving it, one can be fairly certain that it was the drug and not some other factor that caused the improvement.

(b) *The Need for Controlled Studies.* In 1962, the Congress of the United States, after extensive hearings,<sup>4</sup> concluded that testimonial evidence of a drug’s effectiveness—even including testimonials and illustrative “case histories” by physicians—was simply not reliable. It passed the law requiring that effectiveness be shown by “adequate and well-controlled

<sup>4</sup> See, e.g., Hearings on S. 1552 before the Subcommittee on Antitrust and Monopoly of the Senate Committee on the Judiciary, 87th Cong., 1st Sess., pt. 1, at 195, 282, 411-12. For a detailed discussion of the Congressional decision in 1962 to require adequate testing of drugs’ effectiveness, see *Pharmaceutical Manufacturers Ass’n v. Richardson*, *supra*, 318 F. Supp. at 306 et seq.

clinical investigations" which is discussed elsewhere in this opinion.

The Supreme Court examined this issue closely in 1973 and determined that Congress' decision and FDA's enforcement of that decision were supported by the evidence elicited at the congressional hearings:

(The FDA's) strict and demanding standards, *barring anecdotal evidence indicating that doctors "believe" in the efficacy of a drug*, are amply justified by the legislative history. The hearings underlying the 1962 Act show a marked concern that impressions or beliefs of physicians, no matter how fervently held, are treacherous. (Emphasis added.)

*Weinberger v. Hynson, Westcott & Dunning, Inc.*, *supra*, 412 U.S. at 619. It noted:

the conclusion of Congress, based upon hearings, that clinical impressions of practicing physicians and poorly controlled experiments do not constitute an adequate basis for establishing efficacy.

(*id.*, 412 U.S. at 630).

Since both the Congress and the Supreme Court have spoken on this question, no further discussion by the Commissioner of the need for adequate and well-controlled studies,<sup>5</sup> rather than reliance on testimonial evidence, to show a drug's effectiveness is legally necessary. However, there is a continued public

<sup>5</sup> It should be noted that other types of testing are required to show a drug's safety, some of which must be completed before clinical investigations to show effectiveness can begin. (See 21 U.S.C. 355(d).)

belief in testimonial or anecdotal evidence, fostered even by the lawyer of one of Laetrile's supporters. (See oral argument of Kenneth Coe, in which he contends that the safety and effectiveness of Laetrile has been shown by "anecdotes of people who have been diagnosed as terminal with cancer, anecdotes of people who have been cured of cancer, anecdotes of people who are walking around today, that are here today—well" (Tr. at 453). For this reason, the Commissioner will discuss the evidence in the record illustrating the need for scientific studies to show a drug's effectiveness.

In his affidavit (R 175, Ex. A at ¶ 3), Dr. William Beaver, an expert in drug testing, notes that critics of well-controlled studies "often point out the undisputed fact that great strides have been made in therapy in the past without the benefit of this experimental device, but simply on the basis of the uncontrolled observations of astute clinicians \* \* \*. (However), these critics often fail to mention the thousands of drugs which, on the basis of 'clinical experience,' were once accorded an 'indispensable place' in therapy, and which are now known to be useless." Dr. Beaver states (*id.* at ¶ 4): "The function of the controlled clinical trial is not the 'discovery' of a new drug or therapy. Discoveries are made in the animal laboratory, by chance observation, or at the bedside by an astute clinician. The function of the formal controlled clinical trial is to separate the relative handful of discoveries which prove to be advances in therapy from a legion of false leads and unverifiable

clinical impressions, and to delineate in a scientific way the extent of and the limitations which attend the effectiveness of drugs." See also affidavit of Bryant L. Jones (R 431 at ¶ 8): "Most medical mistakes of past centuries were a direct result of beliefs that were predicated on conviction rather than evidence. Most medical advances in modern times can be traced directly to the scientists insistence on valid scientific evidence to support use of today's drugs."

Because of the insidious nature of cancer, it is all the more important that the effectiveness of a drug purported to be useful in the treatment of cancer be demonstrated by well-controlled clinical studies and not solely by testimonials or anecdotes. Cancers in humans vary greatly in their behavior, i.e., their rate of growth, pattern of spread, effects on the normal organs of the person, and the types of clinical symptoms or signs they produce. There is wide variability in the pattern of spread and the outcome for an individual. The effects of cancer on an individual have an element of randomness, that is, an element of chance. Physicians are therefore simply unable to predict the outcome of any cancer at any stage of development with great accuracy. Patients with terrible and widely spread cancer will occasionally have miraculous or unexpected remissions of the disease. Untrained clinical investigators who administer any remedy to a large enough group of patients with cancer will ultimately observe a miraculous outcome. This apparently miraculous outcome may well mislead the untrained investigator into belief that the

remedy was responsible for the result (R 390 at ¶ 14-15).

It has been noted above that, in an adequate and well-controlled study, neither the patient nor the investigator is told that the test drug is being administered because, if they knew, they might report results based merely on high expectations. This problem of assigning improvement to a drug when the improvement was simply a result of high expectations is known as the problem of the "placebo effect." The placebo effect is particularly common in cancer patients. A study of the placebo effect among 288 cancer patients undergoing controlled trials of oral analgesics showed that 112 patients received 50 percent or greater relief from placebo (i.e., non-drug formulations (R 186 at ¶ 13)).

In his affidavit (R 185 at ¶ 20f) Dr. Daniel S. Martin states: "Humans are very susceptible, particularly when ill and desperate with hope, to the power of positive suggestion—namely, when given a 'drug' by an authority figure (e.g., a physician) with the firm statement and promise they will now begin to feel better, to have pain relief, to eat better, and to get well, these hopeful patients frequently do just what they have been told to expect." This, Dr. Martin states "is termed the placebo effect." Dr. Martin also explains that "Cancer is a chronic disease which some patients can live with for years before dying of the disease. During this slow death there are periods of 'ups' as well as 'downs,' and it is not



surprising to have a Laetrile patient ascribe the 'up' to Laetrile, when it was merely coincidental timing" (id.). Similarly, Dr. Carl M. Leventhal states (R 184 at ¶ 7): "(P)sychogenic responses, popularly known as the placebo effect, are well documented and have been shown to occur from 30 to 70 percent of patients who are treated for pain."

The need for controlled testing as opposed to testimonial or anecdotal evidence of effectiveness is well-recognized by experts in the evaluation and use of drugs. As Dr. Baynard H. Morrison states: "The problem is the anecdote doesn't permit you to know what happened yesterday. It doesn't permit you to know what is really going on today and certainly it doesn't give you any insight at all in what will happen to a given patient tomorrow, next week, or next year. To really know what a drug, any treatment, does to a patient you have to be able to evaluate him in the context of a large group whose disease you can follow carefully over a considerable period of time" (Tr. at 150).

(c) *The "Evidence" of Laetrile's Effectiveness.*

(i) *Case Reports.*—The proponents of Laetrile (or amygdalin) have not submitted anything to the record that could be characterized as an adequate and well-controlled clinical study of Laetrile. In the regulation which defines adequate and well-controlled clinical investigations, it is clearly stated that: "Isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered," even as corroborative evidence for

adequate and well-controlled studies (21 CFR 314.111(a)(5)(ii)(c)). Yet that kind of report is the only "evidence" of Laetrile's effectiveness which has been submitted.

Because of the possible public belief in this kind of report, the Commissioner will discuss those submitted to this record. In addition, evaluations, submitted to the record, of earlier "case histories" or testimonials relating to use of Laetrile will be discussed.

(a) Reports Submitted to This Record

(1) Dr. Binzel

Phillip E. Binzel, Jr., M.D., Scientific Advisor to the Committee for Freedom of Choice, and in private practice as a family physician since 1955, appeared at the hearing to make an oral presentation (Tr. at 360-364) and to submit written testimony (Tr. Ex. 13). Dr. Binzel's submission at the hearing (id.) was a report of a study he conducted on more than 200 cancer patients to whom he administered a nutritional program, including Laetrile. Dr. Binzel stated that he had excluded from his report the following patients: "1: Those who were alive but who had been under treatment for less than 4 months. 2: Those who had died within the first 3 months of treatment. These are the patients whose disease was already too far advanced for any form of treatment to be beneficial \* \* \*. 3: Those on whom there is not sufficiently adequate follow-up information to know for certain what their present condition is" (id.).

After the above exclusions, there remained 107 patients in Dr. Binzel's study who had been treated between 4 months and 2½ years and who, according to Dr. Binzel, "are spread pretty equally throughout those time periods" (id.). He reported that 57 patients had primary carcinoma, and 50 patients had proven metastatic carcinoma at the time they started "nutritional therapy" (id.).

Dr. Binzel's exclusion from his study of patients for whom adequate followup information could not be obtained can be expected to exclude those patients who were dissatisfied with Laetrile treatment and left his care. That exclusion, together with the exclusion from consideration of patients who died within 3 months of the first treatment, would be expected to bias the study in favor of effectiveness.

Dr. Binzel states that he "did not attempt to differentiate between those patients who have had surgery and/or cobalt and/or chemotherapy and those who had none of these 'conventional' treatment" (Tr. Ex. 13, "Nutrition and the Cancer Patient" at 2). This, as Dr. Binzel notes, presents a "very valid question." Without knowing whether the patients in whom he saw improvement had had other, recognized effective, treatments, his conclusions cannot be evaluated (cf. 21 CFR 314.11(a)(5)(ii)(a)(2)(iii)).

Dr. Binzel's three-page "study," which was submitted without supporting documentation, simply lacks the details necessary to permit scientific evaluation and would not, for that reason, be considered by experts in drug evaluation even as corroborative

of adequate and well-controlled studies if such studies existed (21 CFR 314.11(a)(5)(ii)(c)).

## (2) Dr. Richardson

Edward Griffin, at the oral argument in this proceeding, submitted page proofs of a book entitled *Laetrile Case Histories. The Richardson Cancer Clinic Experience* by John A. Richardson and Patricia Griffin (Tr. Ex. 1.) Griffin stated: "Previously the opponents of Laetrile have said that there is no evidence that Laetrile works. There has been evidence of course, known to those of us who have been close to the subject. But admittedly, there has not been a great deal of medically documented evidence open to the public. And I believe that with the publication of this book at least we will be able to put an end once and for all to this claim of there not being any evidence" (Tr. at 15-16). Dr. Richardson does not claim to have conducted a research program and his case histories in no way even approximate an adequate and well-controlled clinical investigation.

Dr. Richardson's license for the practice of medicine has been revoked by the State of California (R 183 at 13) because he was found to have discouraged patients from seeking conventional therapy and to have practiced a type of treatment of cancer patients characterized as "an extreme departure from the standard practice of medicine" (R 179, Ex. B at 5). The California State Board of Medical Quality Assurance stated that these two findings established "gross negligence" on the part of Dr. Richardson (id. at 10). Dr. Richardson did not choose to appear in the ad-

ministrative proceeding in which his license was ordered revoked (id. at 1-2).

A number of obvious questions are raised by Dr. Richardson's book: (1) There is no indication in this book—nor is there in the other reports in this section—of the chemical composition of the "Laetrile" which was used. Since there are variations in the composition of the drugs called by the name "Laetrile," this fact leaves the reader with no certainty as to what substance is claimed to be effective.

(2) The technique for selecting patients for reporting is hardly scientific. The book states: "Out of (a group of approximately 4,000 cancer patients), we selected a cross-section of about 500 for our study. We were able to establish contact and a working relationship with only about 250 of these. The cases with the weakest medical histories were discarded, as were those which were overly repetitious. The remainder (62) are contained in the study; but by no means do they represent our entire files" (Tr. Ex. 1 at 118-19).

It is absolutely incredible that anyone would expect to show the effectiveness of a drug by describing 62 out of over 4,000 patients with a selection process of the type Richardson describes. The Commissioner has no means of knowing what happened to the other 3,938 or more patients. No details are given to show how the 500 patients representing a "cross-section" of the 4,000 were chosen. The failure "to establish contact and a working relationship" with half of the patients that were chosen illustrates a serious lack of followup. Logic suggests that those patients who

were not benefited by Laetrile would be less likely to be willing to develop a "working relationship" with Dr. Richardson's office. Clearly patients who had died would not be available for such a relationship. The discarding of weak medical histories has never been an accepted practice in the study of any drug. What constitutes the weakness of a medical history is not explained.

(3) There is some question whether what Richardson claimed to be positive effects were in fact positive. The authors admit that one of the weaknesses of the study is the shortage of cases involving 5-year survival or longer (Tr. Ex. 1 at 120).

Indeed, the case histories section of the book (Tr. Ex. 1 at 126-276) list for each of the 13 different groupings of cancer the expected death rate for those cancers in terms of percentage survival over a set number of years, usually 5 years. Many of the patients simply had not survived long enough at the time of the book's writing to constitute successes.

For example, six cases of female breast cancer are reported (Tr. Ex. 1 at 126-137). According to Dr. Richardson, these women have received metabolic therapy, including Laetrile, for periods varying from 13 to 32 months with an average of less than 21 months. Since Dr. Richardson states (Tr. Ex. 1 at 126): "Two out of every 3 patients with cancer of the breast who do not use Laetrile but choose instead to submit to orthodox therapies will be dead within five years," the fact that he has six patients who have survived 13 to 32 months with a mean of less than



21 months does not provide any evidence of the effectiveness of Dr. Richardson's treatment.

Dr. Richardson recognizes that some of the patients whom he has selected may not have had cancer. See, e.g., Tr. Ex. 1 at 148, patient B1381 where Dr. Richardson, in discussing the chest x-rays of a patient, states that the period of May 73 to January 77 represented: "A three-and-one-half-year remission of *probable* cancer of the lung." (Emphasis added). For several other patients, Dr. Richardson does not quote from the pathology report but merely reports that such a report was positive for cancer (see, e.g., patient P131B (Tr. Ex. 1 at 167)).

(4) Dr. Richardson relies in many instances upon what patients have told him about their medical histories, either orally or in writing. Some patient reports upon which he relies are hardly credible. (See, e.g., patient C106MA (Tr. Ex. 1 at 146): "The patient states the local doctors strongly recommended removal of both lungs and the permanent hospitalization of the patient, who then would be forever dependent on machines to do her breathing.")

(5) Some patient reports are so sketchy as to provide no basis for any conclusion. See, e.g., patient B144J (Tr. Ex. 1 at 202-203: There is no information regarding how the diagnosis of cancer was made. There is no indication that Dr. Richardson ever characterized the size of the tumor or whether he relied on the patient's description. There is no indication whether the patient had received any Laetrile since January 1970. There is no indication that there has

been any contact with the patient since February 1976.

(6) As noted above, for each of the 13 groups of cancer which Dr. Richardson has used in his book he cites the anticipated fatality rates for patients receiving only orthodox treatment. As discussed elsewhere in this opinion, cancers are very different in their behavior, i.e., their rate of growth, their pattern of spread, their effects on the normal organs of the person and the types of clinical symptoms or signs that they produce (R 390 at ¶ 14). Experts in the testing of cancer drugs stress that the effects of cancer on a person have an element of randomness and that the ability to predict the outcome of any cancer at any stage of development varies (*id.*). In light of the regularity with which cancer patients' diseases vary from their expected courses, it would have been surprising if Dr. Richardson were unable to report that 62 out of 4,000 (c. 1½ percent) of patients he saw had remissions for periods of up to, but often much shorter than, 5 years.

Thus, the Richardson book is not only not the kind of adequate and well-controlled clinical investigation necessary to show the effectiveness of a drug, it is not even on its face a particularly credible recounting of medical case histories.

### (3) Dr. McDonald

Lawrence Patton McDonald, M.D., a urologist, and a member of the United States House of Representatives, submitted a statement in which he reported

the following observations after treating almost 200 cancer patients (R 509 at 3):

"(1) Most patients had proven cancer and had had surgery and radiation and/or chemotherapy. Most cases would have been hopeless by routine medical standards.

"(2) Perhaps 30-35% received minimal to no benefit from the program.

"(3) Approximately 40-45% received notable benefits from the program such as improved appetite, improved interest in life, weight gain, lessening or cessation of pain. This category ultimately died but were individually pleased with their improvements.

"(4) About 20% were in the category of marked improvement. In some cases this has been miraculous with these same patients doing very well today."

Dr. McDonald provided no details whatsoever other than those quoted above. Dr. McDonald's report was not, nor does it appear to have been submitted as, an adequate and well-controlled clinical investigation.

#### (4) Dr. Soto

Although Dr. Mario H. Soto appeared and testified (Tr. at 478-481) at the oral argument and was given an opportunity (Tr. at 481) to submit for the record data from his treatment of cancer patients with Laetrile, no data have been received from him.

#### (b) Case Reports Evaluated Previously

Much of the evaluation of case reports has been done in California, where Laetrile originated and was, along with a number of other "unproven" remedies, responsible for the 1959 passage of a State law aimed at cancer quackery. In 1952, the Cancer Commission of the California Medical Association collected information on 44 patients treated with Laetrile, all of whom either had active disease or were dead of their disease, with 1 exception. In some instances, the members of the Cancer Commission had the opportunity of seeing the patients thus treated. The conclusions of the Cancer Commission were that, of those alive with disease at the time of the study, no patient had been found with objective evidence of control of cancer under treatment with Laetrile. Nine patients who died from cancer after treatment with Laetrile were autopsied. Histological studies done for the Commission by five different pathologists showed no evidence of any chemotherapeutic effect (R 378, Att. 15 at 320-326; R 183, Att. 16 at 2-19 and App. 2-3).

In June 1962, the Cancer Advisory Council of the State of California Department of Public Health examined a total of 35 case histories of cancer patients treated with Laetrile. The Council unanimously judged these cases inadequate for any critical evaluation of Laetrile. "Many of the cases had received orthodox treatment; objective evidence of benefit was absent or insufficient, most of the documentation

(dealt) with subjective improvement; some contained no pathological proof of malignancy; many were 1961 cases without followup; the duration of treatment was frequently unknown because the data reported the period of hospitalization only and often discharge dates were not shown" (R 183, Att. 16 at 30-31).

Thirty-six clinical records translated into English from the French were evaluated by the Cancer Advisory Council in December 1962. The Council reached the following conclusions:

1. The records failed to indicate that the patients treated with Laetrile secured either palliation or regression of their cancerous affliction as a result of the therapy.

2. In several instances, there was absolutely no evidence presented as to the response of the patient to the therapy.

3. In other instances, objective evidence documenting the statement of benefits, was not provided.

4. In one group of 17 of these cases, sufficient followup was absent. The longest period of followup was 14 months, 12 days and 23 days of hospitalization. The next longest was 381 days and the last was 127.

5. Results which were reported as "improved" were without meaning since no criteria, subjective or objective, were provided.

6. The evidence presented lends no credence to the alleged efficacy of Laetrile and Vitamin B<sub>15</sub> in the treatment, durative or palliative, of advanced cancer (R 183, Att. 16 at 34-35).

In preparing its 1963 report, the Cancer Advisory Council also reviewed about 16 pounds of documentary material delivered by Laetrile proponents. The material contained a total of 63 case histories, 15 of which were submitted by two doctors in the United States (Dr. Ray Evers, Allusia, Ala., and Dr. John R. Morrone, Jersey City, N.J.).

The opinion [of the Cancer Advisory Council] on review of these cases is that they give no credence to the claimed curative effects of Laetrile in human cancer nor in those animal cancers where it had been investigated. The evidence of palliative response, both subjective and objective, is tenuous and poorly documented. Except in the cases in which death intervened and one or two others in which there was questionable diagnosis of cancer, no followup has been recorded, with the result that the final outcome of the cases is not recorded (R 183, Att. 16 at 35-36).

In January 1963, the McNaughton Foundation and the North End Medical Center, both in Montreal, Canada, submitted to the Cancer Advisory Council of the California State Department of Public Health a total of 14 clinical records on patients treated with Laetrile. These were not complete records but were abstracts furnished by various hospitals in Canada to the McNaughton Foundation. The Cancer Advisory Council appointed a committee of three physicians highly qualified and actively engaged in the treatment of cancer to review and evaluate these records. Each physician made an independent evaluation.



The committee reported: "These 14 records provided by the McNaughton Foundation were examined and fail to indicate that the patient treated with Laetrile secured either palliation or regression of their cancerous affliction as a consequence of the therapy. In several instances, there is absolutely no evidence presented as to the response of the patient to the therapy and in other instances objective evidence which documents claims of benefit is not provided. It is concluded from careful review of these records that they are inadequate as reports of therapeutic use of Laetrile, and they do not indicate that therapeutic benefit resulted from treatment with Laetrile, and do not indicate that this agent is of value in the treatment, cure, or palliation of cancer. In only one instance is there a statement by the examining physician indicating that a definite beneficial effect from Laetrile *might* have occurred" (emphasis in original) (R 378, Att. 14 at 26).

In 1971-72, the FDA, together with the National Cancer Institute, investigated and evaluated 12 clinical histories submitted by Dr. Ernesto Contreras of Mexico covering his experience with Laetrile in the treatment of cancer (see R 184, Ex. 3). FDA was able to obtain documentation covering the full course of the disease in 7 of the 12 case reports. All seven patients whose records were reviewed had received treatment other than Laetrile, including surgery, chemotherapy, or radiotherapy, or more than one of these approaches, either before, after, or concurrently with Laetrile therapy (R 184, Ex. 3; R 198 at 9-10).

Most of the alleged improvements stated, in the 7 case reports which could be evaluated, to be associated with Laetrile treatment have been found to be associated with one or more of the following events in the patient's disease (see R 183, Att. 16 at 10-11):

a. *Subjective improvement* was interpreted as being evidence of the agent's affecting the neoplasm, rather than being due to the general effect on the host, whether by metabolic or psychological reasons.

b. Phases in the *natural history* of malignant neoplasm not infrequently observed in patients who are receiving no treatment whatever were interpreted as being due to the therapy employed (emphasis in original). \* \* \* (For example,) occasional patients with widespread peritoneal carcinomatosis will exhibit regression of their disease following simple exploratory procedures.

c. Patients reported as showing regression of cancer with Laetrile were either receiving concurrent treatment by other methods, or had in their recent past been treated by some (orthodox therapy) and were exhibiting a degree of control of their disease *entirely attributable to the previous treatment* (Emphasis in original). \* \* \*

d. A few of the patients treated did not have proof of the presence of cancer in the form of histological diagnoses, the evidence being more or less inferential, as radiographic observation of lesions in the lung, or a surgeon's diagnosis of a lesion as cancerous on observations of gross pathology at operation, without confirmation with biopsy.

e. Very few of the clinical records to which the Cancer Commission had access contained any sort of satisfactory evidence as to objective, accurate evaluation of the progress of the primary neoplasm or its metastases while under treatment.

(ii) *Animal Testing of Laetrile*.—As indicated elsewhere in this opinion, general recognition of Laetrile's effectiveness among experts in the evaluation of drug effectiveness could only be based upon adequate and well-controlled clinical (i.e., human) investigations. Thus, even if Laetrile had been shown to be effective in animal test systems, and the Commissioner concludes it has not, that fact would not remove Laetrile from the category of "new drug."

Nevertheless, in the interest of providing the public with all the information available in the record concerning this drug, the Commissioner will discuss the animal tests done with amygdalin about which there is controversy. Amygdalin has been extensively tested in animal systems. From the tests done, Dr. Dean Burk, president of the Dean Burk Foundation, Inc., has selected three tests done in the United States as showing a positive effect (R 302). In each case the laboratories which ran the tests found them to be negative. Dr. Burk also cites two foreign reports, one of which was not published (id.). His contentions, and the evidence relating to each in the record, will be discussed point by point and other animal testing done with the drug will be noted.

## (a) Tests Claimed to Show a Positive Effect

### (1) Sloan-Kettering

Dr. Burk includes the following in his list of animal studies showing a positive effect for amygdalin:

Sloan-Kettering Cancer Center (New York), with CD<sub>1</sub>F<sub>1</sub> mice bearing spontaneous mammary carcinomas: Inhibition of formation of lung metastases, inhibition of growth of primary tumors, and greater health and appearance of animal hosts, upon treatment with 1-2 gm crystalline amygdalin/kg body weight/day (Report of K. Sugiura, June 13, 1973) (R 302, Ex. A at 15).

Regarding the studies conducted at Sloan-Kettering, C. Chester Stock, Ph. D., Vice President and Associate Director for Administrative and Academic Affairs, Sloan-Kettering Institute for Cancer Research, stated in his affidavit (R 195) that:

We have tested amygdalin at high doses, 1000 mg/k/day, in over a dozen transplantable tumor systems and one induced tumor system without seeing any action against the tumors. The chemotherapeutic agents effective in clinical cancer have not had or would have had their activities detected in one or more of those systems.

In spite of demonstrated utility of transplanted experimental animal tumor systems, some individuals believe that use of spontaneous animal tumors is more appropriate for seeking drugs for use in man. It was considered that this

would be true of the advocates of the use of Laetrile who believe it needs to be used for relatively long periods of time.

Consequently, Dr. K. Sugiura in my laboratory looked for the effects of amygdalin on the growth of spontaneous mammary tumors in CD<sub>1</sub>F<sub>1</sub> mice and also on metastatic spread to lungs of the hosts. Early observations of Sugiura featured an apparent inhibition of the appearance of metastases in the lungs of mice given daily (except Sunday) doses of 2000 mg/k of amygdalin in his 3 initial experiments. The treated mice showed lung metastases in 20% while 80% of the controls had metastases. The mice had been injected until death or until the primary tumors were over 2.5 cm in diameter. The data from these experiments were leaked to the press unfortunately before they could be checked adequately. Subsequent experiments, in some of which Dr. Sugiura participated, some conducted with Dr. Daniel Martin of the Catholic Medical Center of Brooklyn and Queens and some which were independent by other investigators in our Institute, showed that the initial results were not consistently observable. In some experiments there were more metastatic mice in the treated than in the control mice. In the latest experiment in which Dr. Sugiura read the lungs of the mice without knowing what treatment they had received, there was essentially no difference found between the treated and control groups (R 195 at ¶ 10).

In his affidavit (R 185), Daniel S. Martin, M.D., states that: "My laboratory's tests with Laetrile

demonstrated Laetrile to be without effect (on spontaneous tumors in experimental animals). Further, these negative tests on these animal tumors were confirmed by three other investigators at Memorial Sloan-Kettering Cancer Center in New York. One of the latter investigators (Dr. K. Sugiura) reported his initial experiments to demonstrate Laetrile to have anti-cancer activity, but his subsequent results were negative. A degree of variability in results is common in biological research, and the final opinion is based on whatever the majority of the findings are. In this instance, the totality of the data clearly and unequivocally reveals Laetrile to be without anti-cancer activity" (R 185 at ¶ 21(c-d)).

## (2) Southern Research Institute

Dr. Burk's citations continue:

Southern Research Institute (Birmingham, Alabama) for the National Cancer Institute, in a majority of 280 BDF<sub>1</sub> mice bearing Lewis lung cancers, treated with up to 400 mg crystalline amygdalin per kg body weight, with respect to increased life span (Report, December 3, 1974) (R 302, Ex. A at 15).

The results of two studies conducted by Southern Research Institute for the National Cancer Institute were published in the scientific literature in 1975. One of the studies involved an experiment "in which four transplantable rodent tumors (L1210 lymphoid leukemia, P388 lymphocytic leukemia, B16 melanoma,



and Walker 256 carcinosarcoma) were used to investigate the antitumor activity of amygdalin MF \* \* \* alone and in combination with *beta*-glucosidase" (R 184, Ex. 3b at 939). No antitumor activity was observed in any of the four tumor systems tested with amygdalin alone or in combination with *beta*-glucosidase (*id.*; see also R 173, Att., Memorandum, March 12, 1973).

The second study, in which amygdalin MF (i.e., amygdalin provided by the McNaughton Foundation) was evaluated alone or in combination with *beta*-glucosidase against three transplantable rodent tumors (Ridgeway osteogenic sarcoma, Lewis, lung carcinoma, and P388 leukemia), showed that amygdalin alone or in combination with *beta*-glucosidase did not demonstrate antitumor activity against any of these three tumor systems (R 184, Ex. 3C at 952-53).

At the oral argument, Bayard H. Morrison, M.D., Assistant Director at the National Cancer Institute stated that the Institute:

has sponsored—other organizations have conducted—tests of Laetrile at various dosage levels in a variety of animal tumor systems, probably exceeding 15 or more, probably closer to 20.

This indeed really is about the most extensive that NCI and other laboratories in the aggregate have tested of essentially a nonactive substance. For in all of these tests which include tumors ranging from carcinomas, sarcomas, lymphomas, any kind of tumor which parallels to a large degree the human type of tumor, the results have

been essentially negative. There have been occasional, marginal evidences of activity which have not been reproducible.

So, in balance, Laetrile has failed the test of demonstrating activity in the preclinical animal tumor systems that we know now predict for activity in human cancer.

And I should add that of the 30 or 40 drugs that are now regularly available and known to have effect in certain forms of human cancer, all of these drugs have demonstrated activity, significant activity, in one or more of these animal tumor systems (Tr. at 146A-47).

The proponents of Laetrile question the statistical controls and experimental design employed in the studies conducted by Southern Research Institute (see R 302, Ex. E). They suggest the utilization of methods of statistical analysis developed for use in judging results obtained with physical, rather than biological, systems. One of the research scientists at the National Cancer Institute responsible for the studies conducted by Southern Research Institute points out that "[t]he variation in all biological systems is far greater than that involving physical phenomena" (R 438 at 1). He suggests that it is, for that reason, not possible to use the internal statistical analyses suggested by the proponents of Laetrile (*id.*).

## (3) Scind Laboratories

Dr. Burk's third reference is:

Scind Laboratories, University of San Francisco, 400 rats bearing Walker 256 carcinoma (200 treated with amygdalin, 200 controls), with 80 percent increase in life span at optimum dosages (500 mg amygdalin/kg body weight) (October 10, 1968). Cf. FDA-IND application No. 6734, pp. 247-8, 00080-00093 (R 302, Ex. A at 15).

The Scind Laboratory data were submitted to FDA in support of the McNaughton Foundation's IND for amygdalin in 1970. An ad hoc committee of cancer experts evaluated these data during its review of the IND. In its report, the Committee stated: "We are particularly cognizant of the lack of adequate evidence of *in vivo* antineoplastic characteristics. The Scind Laboratory data in the initial submission of IND 6734, April 6, 1970, concerning two experiments with a Walker 256 system are considered unacceptable because of inadequate documentation of status of animals, percentage of tumor take, rate of growth, and accounting for acute deaths[,] and the other substantial lack is a statistical analysis. Scind Laboratory, in a letter dated October 18, 1968, filed with [an] October 31, 1970, amendment, states 'Laetrile, when administered without Beta glucosidase has *little or no effect* upon transplanted rodent tumor systems tested.' (emphasis theirs [i.e., Scind Laboratory's])" (R 184, Ex. 2 at 1).

## (4) Pasteur Institute

Dr. Burk's fourth reference is:

Pasteur Institute (Paris), with human cancer strain maintained in mice treated at optimal dosage of 500 mg Amygdalin Marsan/kg body weight/day; increased life span and delayed tumor growth up to 100 percent (Dec. 6, 1971 report by M. Metianu) (R 302, Ex. A at 15).

In a sworn affidavit (R 422), a medical officer in the Bureau of Drugs, who is trained in medicine and experienced in scientific research and who is fluent in both French and German, commented on the cited studies conducted at the Pasteur Institute in Paris and the Institute von Ardenne in Dresden (see discussion below).

The medical officer, through the American Embassy in Paris, learned that the report entitled, "Anti-Tumor Toxicity and Activity" was written on the letterhead of the Institute Pasteur and was an internal report of the Institute that has never been published in any scientific journal. In the affidavit, the medical officer states that the fact that the report "represents preliminary work only and has not been published in any scientific journal since it was prepared six years ago raises my suspicions that the preliminary results obtained could not be reproduced" (R 422 at ¶ 6).

## (5) Institut von Ardenne

The fifth reference cited by Dr. Burk is:

Institut von Ardenne (Dresden, Germany). H strain mice bearing Ehrlich ascites carcinoma treated with bitter almond amygdalin ad libitum in addition to the regular chow diet: increased life span and decreased rate of cancer growth, treatment beginning 15 days before cancer inoculation (Arch. Geschwulstforsch 42, 135-7, 1973) (R 302, Ex. A at 15).

After reviewing the article published in the Arch. Geschwulstforsch, the Bureau of Drugs medical officer made the following comments:

The author's terms (in the summary section) "feeding with bitter almonds," "prolongation of survival" (due to feeding with bitter almonds), and "inhibition of tumor growth" are not adequately defined in the subsequent text or by the content of the text and thus are uninterpretable.

The description of the methodology is deficient for a number of reasons. It fails to provide information whether the mice were kept singly or caged in groups. It fails to provide information on the techniques for demonstrating whether and how much of the bitter almonds had been eaten by each experimental mouse. It fails to inform on the origin, quality, and composition of the bitter almonds with respect to the latter alleged role of "amygdaline" and HCN. Due to these failings it is not possible to draw conclusions from any differences of events between experimental and control animals—if such differences could be demonstrated at all. The author also fails to give the age of the mice and the body weight of each individual mouse of each group

and at each weighing date. The use of sole mean values in this paper is potentially misleading. (The scientific evaluation of data requires implementation of variabilities of the individual measurements.)

The author makes statements on "tumor growth" which are based on implications, indirect deductions, and on arbitrary assumptions.

The term "tumor growth" is potentially misleading for the Ehrlich ascites cancer which consists of a cancer cell suspension in the peritoneal fluid. The study fails to use precise methods of measuring the number of cancer cells present in each mouse.

\* \* \* \* \*

In my opinion, this article fails to provide any evidence that bitter almonds are effective in inhibiting the growth of tumors (R 422 at § 7).

#### (b) - Other Tests

As noted above, the two tests done by the Southern Research Institute and the Sloan-Kettering studies now completed have demonstrated conclusively, in the view of most experts, that amygdalin, either alone or in conjunction with the enzyme *beta*-glucosidase, exhibits no antitumor effect. These results are in accord with the negative findings of three earlier animal studies commissioned by the National Cancer Institute. Those tests are summarized in the record as follows:



1957: Amygdalin was tested with three transplanted mouse tumor systems used at the time by the NCI Cancer Chemotherapy National Service Center (CCNSC) to screen compounds for anti-cancer activity. Amygdalin produced no significant inhibition or growth of the carcinoma 775 or sarcoma 180 tumors, and produced no significant increase in the lifespan of mice with leukemia L1210 tumors.

1960: Material from a different source was tested against the same three mouse tumors. The compound failed to show antitumor activity.

1969: Amygdalin was tested alone and in combination with beta-glucosidase against leukemia L1210 in mice. Amygdalin was inactive against the tumor, alone and in combination with the enzyme. Toxic side effects increased when the drug and enzyme were given together (R 173, Att., "NCI Testing of Laetrile (Amygdalin)").

A study, entitled "Failure of Amygdalin to Arrest B16 Melanoma and BW5147 AKR Leukemia," Hill et al., Cancer Research, 36:2102-07, June 1976, appears as Exhibit 3 to R 170. The December 9, 1976 report of yet another animal test of amygdalin is Exhibit 3D to R 184. The drug was found not to be active against human breast and colon tumor xenografts in athymic mice.

The failure of Laetrile (or amygdalin) to show any effect in animal systems is important because those systems have shown an ability to predict effectiveness in humans. See the statement of Dr. James F. Holland (R 356): "No drug has been proved ac-

tive in human cancer which does not show anti-cancer activity in experimental animals. Human cells are not so different from other mammalian cancer cells that an active drug does not act on at least one other mammalian system \* \* \*. Laetrile is completely inactive against animal cancers. It has been repeatedly tested in reputable laboratories against a broad spectrum of rodent neoplasms. Inasmuch as no drug has been found active against cancer which isn't active in the screening tumors, there is no basis to consider Laetrile a candidate chemotherapeutic compound against human cancer \* \* \*. No scientifically accepted data whatever have been presented indicating evidence of benefit from Laetrile."

See also the statement of Dr. Bayard H. Morrison, Assistant Director of the National Cancer Institute: "[O]f the 30 or 40 drugs that are (now) regularly available and known to have effect in certain forms of human cancer all of these drugs have demonstrated activity, significant activity, in one or more of these animal tumor systems." (Tr. at 147).

One comment theorized that the reason why animal tests do not show Laetrile to have any anticancer activity is because the laboratory animals are bred to have defective immune rejection systems (R 235 at 7). This theory assumes that Laetrile is hydrolyzed by an enzyme that is in greater concentration at the cancer site than at other locations in the body. The comment explains that: "If, because of a defective immune system, laboratory animals produce no hydrolyzing enzyme at the cancer, (sic) site, that fact

alone would explain why Laetrile doesn't work on laboratory animals. It can't work on any organism that has a defective immune system.'” (See R 235 at 7-8). No evidence has been submitted to support the comment's theory.

The Commissioner concludes that the animal studies conducted to date fail to show that Laetrile (or amygdalin) has anticancer activity in laboratory animals. As has been noted previously, even if these tests showed that the drug had anticancer activity in laboratory animals, such findings would not be relevant to the question whether it is generally recognized by qualified experts as a safe and effective anticancer drug, since general recognition must be based upon testing in human beings. The lack of positive effect in test animals is of some importance, since a clear showing of success in animals might suggest the propriety of clinical testing in humans. The failure of amygdalin to produce an anticancer effect in animals is added reason for skepticism concerning the claims that it is effective in humans.

## 2. *Testimony of Experts*

(a) *Experts Opposed to Laetrile.* The evidence that experts in the evaluation of drug safety and effectiveness do not “generally” recognize Laetrile as effective for any therapeutic use is overwhelming. (It should be remembered that for recognition to be general it must be shown that most qualified experts recognize the drug's safety and effectiveness. The fact that a few persons claiming expertise believe the drug safe and effective is thus not sufficient.) The

record contains statements that Laetrile is not considered as an effective cancer therapy from several organizations with members who are experts in cancer drug evaluation—e.g., the American Cancer Society, the American Medical Association, the Committee on Neoplastic Diseases of the American Academy of Pediatrics—and from a large number of the Nation's most eminent and well-qualified experts in the area of cancer drug evaluation. It is difficult to conceive of a clearer showing of a lack of “general” recognition of a drug's effectiveness than the expression of the views of these many experts.

The Commissioner will describe the qualifications of some of these experts and either quote from or summarize the views which they have expressed. Each of the submissions referred to contains a great deal of information concerning Laetrile and the consensus of expert opinion about it, and the following excerpts are meant only to be illustrative of the views each expert expressed:

Arthur I. Holleb, M.D., Senior Vice President for Medical Affairs, American Cancer Society, Inc., submitted an affidavit (R 173). His curriculum vitae lists his membership in and leadership of several professional societies, which include the James Ewing Society and the American Radium Society. He also serves on the Cancer Commissions of the American College of Surgeons and the American College of Radiology and is editor-in-chief of CA, a cancer journal published by the American Cancer Society.

Dr. Holleb stated (R 173 at ¶ 3) that he had reviewed three basic documents attached as exhibits to his affidavit and supporting documents for these basic documents and that the information contained therein was true and correct. Submitted as an attachment to Dr. Holleb's affidavit is a "Statement Concerning Laetrile" by Frank J. Rauscher, Jr., Ph. D., Former Director, National Cancer Program, National Cancer Institute. Dr. Rauscher states, "There is no evidence that Laetrile works. Over the last decade, or more, NCI has repeatedly conducted tests of Laetrile in a variety of animal tumor systems. Most have been completely negative. The others have shown only marginal levels of activity which could not be reproduced. The animal systems used are those which have detected the active properties of the scores of drugs which, unlike Laetrile, have proven to be of demonstrable value in patients with many forms of cancer. The therapeutic benefits as well as the attending side effects of these materials have been clearly and amply documented in clinical literature based on carefully conceived, meticulously conducted and monitored clinical trials. The same cannot be said for Laetrile where clinical reports are largely anecdotal and unsubstantiated. Thus, there is no laboratory or clinical evidence of the effectiveness of Laetrile" (id. at 2).

See also testimony of R. Lee Clark, M.D., President, American Cancer Society, in which he states: "The American Cancer Society views Laetrile as hav-

ing no proven value in the treatment of human cancers. The Society has made a continuing review of all the literature and other information available and finds no evidence that treatment with Laetrile results in objective benefits to patients with cancer. Since 1956, the National Cancer Institute, in conjunction with the cancer research centers of America, has reviewed over 300,000 drugs, chemicals, antibiotics, and other agents including Laetrile to evaluate them in regard to their usefulness in cancer treatment. From this research, more than forty specific agents have been found to have an effect against cancer in animal and in man. Although several trials have been made with Laetrile, it has never been proved effective in cancer in any way whatsoever" (R 307 at 1).

Frederick N. Silverman, M.D., Chairman, Committee on Neoplastic Diseases, American Academy of Pediatrics, submitted testimony (R 233 and 317) which included the following comments from his committee: "Laetrile has never been shown to exhibit any efficacy in the treatment of neoplastic disease in children. It cannot be regarded as safe if it is used in lieu of drugs currently employed either as accepted treatment or in carefully designed investigative treatment protocols."

William R. Barclay, M.D., testified (Tr. 269-281) for the American Medical Association (AMA). The AMA supports the "FDA's contention that laetrile is a new drug and is neither generally recognized by experts as safe and effective for its purported use



nor should (it) be distributed in interstate commerce until such time as its safety and efficacy for the treatment of cancer have been established through controlled preclinical and clinical studies" (Tr. at 272).

Dr. Barclay discussed (Tr. at 274) a May 1965 report in the Canadian Medical Association Journal which "concluded that laetrile could not be considered as a palliative cancer therapy on the basis of the biological rationale advanced by the manufacturer." He further states that: "the American Cancer Society has long pointed out through its continuous reviews of the scientific literature that laetrile is not a proven or generally recognized treatment for cancer. The American Medical Association likewise views laetrile as ineffective in the treatment of cancer" (Tr. at 275-276). At its 1976 Clinical Convention, the AMA adopted the following resolution pertaining to the profession's view of Laetrile: "*Resolved*: That the American Medical Association continue to inform the public of the danger of delay in the diagnosis and treatment of malignancies by methods not generally recognized by the medical profession as beneficial and effective; and be it *Further resolved*, That the American Medical Association inform the public that the safety and efficacy of amygdalin for the treatment or palliation of malignancies is unproven and that the use of amygdalin in such cases exploits the victims of malignancies and their families by preying upon the emotions of the hopelessly ill, in some cases for the profit of the unscrupulous." Dr. Barclay (Tr. at 276) states: "We believe that experts qualified

by scientific training and experience to evaluate the safety and effectiveness of drugs are virtually unanimous in their recognition of the ineffectiveness of laetrile for the treatment of cancer." The AMA testimony concludes (Tr. 280): "It is clear that laetrile is not generally recognized by experts qualified to evaluate the safety and effectiveness of drugs as safe and effective."

W. Sherwood Lawrence, M.D., a Medical Officer of the State of California Department of Health, Public Health Division, Food and Drug Section, serves as the Executive Secretary of the State of California Cancer Advisory Council. He is the custodian of the records of the Council and is knowledgeable of the work of the Council and the study that the Council has conducted (R 183 at 1). Dr. Lawrence states (R 183 at 17): "The evaluation by the Council of all the clinical data available here and in Canada has failed to establish any evidence of clinical efficacy. The proponents have never published competent well-designed controlled clinical studies demonstrating the slightest efficacy of Laetrile in the cure, amelioration or control of cancer. Laetrile (amygdalin) is not generally recognized by qualified experts as either safe or effective in cancer therapy."

Jonathan E. Rhoads, M.D., is National Chairman of the National Cancer Advisory Board, a surgeon, former President of the American Cancer Society and a member of a number of organizations focusing on research, including the American Association for Cancer Research and the American Institute on Nutrition.

He made a presentation at the oral argument (Tr. at 109-115), on behalf of himself, as a citizen, and the American Cancer Society. Dr. Rhoads stated (Tr. at 114): "The position of the American Cancer Society is that Laetrile can be toxic in some doses and some modes of administration. But that more importantly, it is unsafe because its effectiveness has not been demonstrated scientifically so that reliance on it may lead patients to forego better treatment. Laetrile certainly has not been proven effective as a cancer treatment or cure and is not generally recognized by qualified experts as safe and effective for cancer."

Jesse L. Steinfeld, M.D., is Dean of the School of Medicine, Medical College of Virginia, Richmond, Va.; he was formerly Deputy Director of the National Cancer Institute; United States Surgeon General; Deputy Assistant Secretary for Health and Scientific Affairs, Department of Health, Education, and Welfare; and Chairman of the Department of Oncology and Director of the Comprehensive Cancer Center at the Mayo Clinic. His professional experience includes over 20 years of involvement in cancer research, particularly with respect to the metabolic effects in cancer patients that occur as cancers grow and metastasize (R 194). Dr. Steinfeld was recognized as an expert in the evaluation of the safety and effectiveness of cancer drugs by the Court in *Durovic v. Richardson*, 479 F.2d 242, 248 (7th Cir.), cert. denied 414 U.S. 944 (1973). He states that neither amygdalin nor any other cyanogenic glycoside

is generally recognized by himself or by experts generally, to be safe and effective for any medical purpose (id. at 5). Dr. Steinfeld also states: "I have reviewed the clinical records of a number of patients who have received laetrile as treatment for cancer, while I was in California. In that review, there was no evidence to support the view that laetrile was of value to cancer patients. I have reviewed the volumes of material submitted to the FDA in 1970, requesting an Investigational New Drug Application (IND) for laetrile. The application was not approved because of serious flaws or deficiencies in both the animal and human trials" (id. at 8).

Richard H. Lange, M.D., is Chief, Section of Nuclear Medicine, Ellis Hospital, Schenectady, N.Y. He submitted verified testimony (R 385) in which he cited his experience in the field of internal medicine, nuclear medicine, and his particular interests in the problem of cancer. Dr. Lange states: "When one reviews the extensive information presently available from leading experts on cancer, there is no evidence to suggest that Laetrile is in any way an effective cancer drug \* \* \* The theory that Laetrile is effective because it destroys cancer cells by producing a release of cyanide has never had any scientific support, nor has the newer claim in the prior approach that cancer is caused by a vitamin B-17 deficiency and that Laetrile is vitamin B-17. No scientific group has recognized Laetrile as a vitamin. \* \* \* Evidence of an anti-tumor effect in animals must be suggested or proven before a drug can be used in human clinical

cal trials. Without such proof of effectiveness, the concept of scientific investigation would be altered; the gates would be open to all sorts of quacks and utter confusion would result. Placebo effects and personal testimonials must be separated from competent objective scientific investigation which is free from bias, personal prejudice or emotional involvement" (R 385 at 1-2).

Michael B. Shimkin, M.D., is Professor of Community Medicine and Oncology, School of Medicine, University of California, San Diego, and has had 40 years of experience in cancer research, teaching, and clinical treatment of patients. He has authored or co-authored over 280 publications on clinical and laboratory cancer research (R 192). Dr. Shimkin states: "My knowledge about amygdalin ('Laetrile') spans some 30 years. At no time, nor now, has there been evidence that this material is useful in the prevention or treatment of cancer in man or in experimental animals. I know of no expert of cancer in chemotherapy who has evidence of usefulness of amygdalin in the treatment of cancer, nor of any recognized journals or textbooks in medicine that indicate such usefulness. I know of no laboratory or clinical studies of amygdalin that demonstrate scientifically any significant, repeatable benefit in animals or in man" (id. at ¶ 12).

Bernard C. Korbitz, M.D., is Chief of the Chemotherapy Section, Department of Oncology at the Radiologic Center, Inc., Nebraska Medical Hospital, Omaha, Nebr. He has been involved in various as-

pects of cancer research and cancer therapy since approximately 1954. His professional training and experience includes the authorship or co-authorship of approximately 40 articles relating to cancer hematology and internal medicine (R 181). Dr. Korbitz states: "To date, there has been no bona fide or substantiated evidence that Laetrile has any significant anti-tumor effect in any of the rodent animal systems evaluated. I have reviewed reports by Dr. Navarre in the Philippine Medical Journal who purported to have produced good results in cancer patients using larger doses. In reviewing his studies there is no objective evidence to support these claims that Laetrile is effective in any dose range against cancer" (id. at 3). Dr. Korbitz also states, "There is no objective evidence of any sort from pre-clinical or sketchy clinical reports to indicate that Laetrile has any benefit in the treatment of cancer patients" (id. at 4).

Susan J. Mellette, M.D., is Associate Professor of Medical Oncology, Medical College of Virginia and has had over 20 years experience in a private practice essentially limited to patients with metastatic malignant diseases. In 1975 she was President of the American Association for Cancer Education, an organization of medical and dental school faculty interested in cancer teaching in professional schools (R 420). Dr. Mellette states, "My views on the substance Laetrile are based on reports of the ineffectiveness of amygdain which have been published in the standard scientific literature and also on two books and other printed materials put out by proponents of Laetrile which I have read. In the latter,



I have found only unsubstantiated testimonials and hearsay in the patient reports and so-called scientific arguments which reach unwarranted conclusions without appropriate experimental methodology" (R 420 at 1).

Daniel S. Martin, M.D., has been involved in general cancer research since 1946. Since 1950, he has worked in cancer chemotherapy, and since 1958 in cancer immunology as well. His professional bibliography includes over 100 publications, the vast majority of which resulted from research in cancer immunology and chemotherapy (R 185). Dr. Martin states, "The proponents of Laetrile claim that their clinical studies in cancer patients demonstrated that Laetrile often reduced the size of a malignant tumor and caused some tumors to completely regress. *Evidence*—none; i.e., no *objective* evidence to support such a claim. No 'hard' patient data, no tumor measurements of the progress of the disease state, no biochemical data, no survival data, etc. The pro-Laetrilists do not present any competent scientific evidence that Laetrile is effective for the treatment of cancer. Only testimonials—'anecdotal' evidence—are presented that the Laetrile-cancer patients and their doctors 'believe' in its efficacy. Belief, however, is not adequate for reliance of drug efficacy. Only strict scientific standards should be employed: namely, adequately documented scientific, well-controlled, evidence of objective antineoplastic effects in humans. The fact that a great many cancer patients have received Laetrile and attest to its benefits is not evidence. Mere clinical experience *per se* is not a sub-

stitute for lack of appropriate objective documentation of clinical efficacy" (emphasis in original) (id. at ¶ 20e).

Harold James Wallace, Jr., M.D., is Director of Cancer Control and Rehabilitation at Roswell Park Memorial Institute, Buffalo, N.Y. He has had extensive training in the clinical pharmacology of cancer drugs and has participated directly in the clinical testing of a number of new anti-cancer drugs. He has, over the past 20 years, conducted and published the results of controlled clinical trials of drugs, radiation therapy, and other treatments of cancer (R 199). He is a cured cancer patient (Tr. at 170). Dr. Wallace states: "There is no evidence in either animal models or in the large numbers of patients who have received amygdalin that it is effective in any way in preventing cancer, causing a regression or remission of cancer, or improving the life expectancy of the cancer patient. Neither has there been any evidence that it decreases the symptoms of pain, weakness, or depression from cancer in any direct way. It is not analgesic or antiemetic in character. The anecdotal evidence claimed by amygdalin proponents has not been presented to me or to any scientific forum for critical review and these claims have not been substantiated by documentation in medical records available for review" (R 199 at ¶ 14).

John T. P. Cudmore, M.D., is a Board-certified surgeon whose professional experience includes the practice at oncology for the past 20 years. Dr. Cud-

more stated that his work requires him to be acquainted with the literature related to drugs used in the treatment of cancer published in professional journals, and that he regularly attends meetings of experts at which drugs used in the treatment of cancer are discussed and evaluated (R 178). Dr. Cudmore states (id. at ¶ 10): "In my practice of oncology in San Diego since 1956, I have examined numerous patients after their treatments with amygdalin or Laetrile in nearby Tijuana, Mexico. I have never seen any evidence of cure or palliation with Laetrile. I can conclude from my personal experience that Laetrile or amygdalin is ineffective in the treatment and prevention of cancer." In support of these statements, Dr. Cudmore discusses in his affidavit the case histories of nine patients who have received Laetrile, all of whom in his opinion received no benefits therefrom. Dr. Cudmore states (id. at ¶ 8): "The composition of amygdalin is such that I do not recognize it, nor is it generally recognized by experts qualified through scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for the use in treatment or prevention of cancer."

Sidney Weinhouse, Professor of Biochemistry at Temple University School of Medicine, is a researcher in the field of cancer for the past 30 years, editor of the journal, Cancer Research, and a member of the Board of Directors of the American Cancer Society (R 384). He made the following statement regarding Laetrile: "Although widely touted for its

curative effects on cancer for many years, there is no shred of evidence from any reputable cancer researcher that this substance has any therapeutic value. I know of no reputable scientist who has published evidence for the effectiveness of Laetrile" (id. et 1).

Bryant L. Jones, M.D., is a Medical Director in the Commissioned Corps of the United States Public Health Service (R 431). Since 1960, first in the pharmaceutical research industry and then in government, he has worked with the design and evaluation of clinical investigations, the purpose of which were to determine the safety and effectiveness of drugs (id. at ¶ 2). Dr. Jones states, "I am presently responsible for the review and evaluation of protocols and reports concerning the use of drugs subject to New Drug Applications (NDA's) and Notices of Claimed Investigational Exemption for New Drugs (IND's). I review such protocols and reports for the purpose of determining whether or not they provide scientifically acceptable standards of safety and effectiveness. I would estimate that I have reviewed several thousands such reports, most of which were and are directly related to and involve drugs intended for use in the field of oncology, which is the management of cancer" (id. at ¶ 3). Dr. Jones states, "I have made a careful review of the statements which are part of the record in this proceeding identified as:

1. Comments: C0001 through C0247.
2. Testimony: TS 01 through 14.

3. Letters: Let No. 1 through 49.
4. Oral arguments: OR 01 through 11.

(When submissions were received by the Hearing Clerk, they were assigned both a number-letter code (used here by Dr. Jones) and an R number, utilized for purposes of citation in this opinion.) I have evaluated each statement and report which purports to show that Laetrile, amygdalin, or any of the cyanogenetic glycosides are safe or effective in the treatment of cancer, as a palliative, as an analgesic, or for any medical purpose. None of the statements or reports are adequate, well-controlled scientific studies. The reports I have examined fail to measure up to the principles applicable to adequate, well-controlled scientific studies in every particular. The studies not only fail to measure up to minimum standards applicable to adequate, well-controlled scientific studies, but also fail to present any scientifically acceptable, objectively documented clinical evidence of safety and effectiveness for amygdalin, Laetrile, or any cyanogenic glycoside" (id. at ¶ 6).

George J. Hill, II., M.D., is Professor and Chairman of the Department of Surgery and Associate Dean for Clinical Affairs of the Marshall University School of Medicine, Huntington, West Virginia (R 170). His professional duties involve the medical management of cancer and require that he be familiar with drugs that are generally recognized as safe and effective in treating cancer. He keeps abreast of the consensus of informed opinion by reading medical

literature concerning cancer and its management, by attending meetings of experts where methods of treatment that are recognized as safe and effective are described and discussed, and through teaching, conducting research, and exchanging views with his colleagues who are experts in the field (id. at ¶ 12). He has himself conducted studies on amygdalin, the reports of which have been published and are attached as Exhibits 2 and 3 to his affidavit. He states, "In the course of my investigation of amygdalin's potential as an antitumor agent, an extensive review of both popular and scientific literature relating to it and Laetrile was conducted. Most reports in the scientific literature supporting Laetrile have appeared in foreign medical journals. Only one preliminary report purporting to support use of Laetrile was found in an American journal. The favorable reports concerning clinical use of Laetrile or amygdalin were testimonials based on individual case reports. There were no adequate, well-controlled clinical studies which demonstrated or purported to demonstrate that amygdalin or Laetrile were safe and effective for use in the medical management of cancer. Neither were there any favorable clinical reports in which an attempt was made to measure any objective parameters for adequate periods of followup to determine any possible drug-induced effect. The literature also contains reports concerning a limited number of carefully monitored clinical cases in which use of amygdalin failed to result in any objective benefit in the management of cancer" (id. at ¶ 9-10). Dr. Hill also



states, "The composition of amygdalin is such that I do not recognize it, nor is it generally recognized among experts qualified through scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use in cancer management, or for any other known medical use. I know of no medical school where use of amygdalin for treatment or prevention of cancer is taught. I know of no medical expert qualified through scientific training and experience in the control of cancer who advocates use of amygdalin" (id. at ¶ 13).

Vincent T. DeVita, Jr., M.D., is Professor of Medicine at the George Washington University School of Medicine, Washington, DC, and is a diplomate of the American Board of Internal Medicine, with subspecialty, certification in Hematology and Medical Oncology (R 169). Dr. DeVita has been Director of the Division of Cancer Treatment, National Cancer Institute, since 1974. His job requires that he regularly attend meetings of experts at which drugs used in the treatment of cancer are discussed and evaluated and that he be acquainted with the literature published in professional journals relating to drugs used in the treatment of cancer (R 169 at ¶ 1-16). Dr. DeVita states (id. at ¶ 18-19), "The composition of amygdalin is such that I do not recognize it, nor is it generally recognized by experts qualified through scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use in the treatment or prevention of cancer.

I know of no adequate, well-controlled clinical study which shows it to be safe and effective for use in the treatment or prevention of cancer in humans. I know of no medical school where use of amygdalin is taught, and of no recognized medical text which prescribes, recommends, or suggests its use. Neither do I know of any expert in cancer chemotherapy who is of the opinion that it is useful in the treatment or prevention of cancer, or that there is evidence that it is useful in the medical management of cancer."

R. L. Meckelnburg, M.D., is Director, Department of Nuclear Medicine, Wilmington Medical Center, Wilmington, Delaware, and a physician concerned with the care and treatment of cancer patients by means of chemotherapy (R 154). He described his limited experience with treating patients with Laetrile in the years 1963-1967. Although Dr. Meckelnburg states (and the Commissioner agrees) that the study was not a clinically controlled series, he reports that "the results of these treatments were uniformly unsuccessful." Dr. Meckelnburg noted, "The individuals who were most interested in promoting the use of Laetrile failed to administer the drug in a manner consistent with good clinical investigative methodologies, particularly the use of the double blind control and crossover models of study." He concluded, "The promulgation of the drug as a preventive for cancer in the light of today's knowledge is totally absurd" (id.).

Robert C. Eyerly, M.D., is a physician and surgeon on the staff of the Geisinger Clinic in Danville, Penn-

sylvania, and a diplomate of the American Board of Surgery (R. 167). He currently serves as Chairman of the Committee on Unproven Methods of Cancer Management, American Cancer Society. This Committee's chief concern is, "With methods that are promoted as having established value in diagnosis, prevention, treatment, or control of cancer, despite a lack of competent scientific evidence to support claims made for them. The Committee reviews material assembled by its staff, mostly from published sources, to find out what kind of claims are made, and they evaluate scientific literature to see if it contains evidence to support such claims" (id. at ¶ 5-7). Dr. Eyerly states, "The composition of amygdalin is such that I do not recognize it, nor is it generally recognized by experts qualified through scientific training and experience to evaluate the safety and effectiveness of drugs as safe and effective for administration to humans for the treatment or prevention of cancer, or for any other purpose" (id. at ¶ 10).

Several experts qualified by scientific training and experience in the field of cancer research and cancer treatment submitted similar statements attesting that they knew of no cyanogenic glycoside that is generally recognized as safe and effective for the treatment, prevention, or cure of cancer, for the relief of pain associated with cancer, or for any medical purpose. They also stated that the composition of these cyanogenic glycosides, in general, and of amygdalin, in

particular, is such that they do not recognize them, and the cyanogenic glycosides are not generally recognized among experts qualified through scientific training and experience to evaluate drugs, as safe and effective for the treatment of cancer, for prophylaxis against cancer, for relief of pain associated with cancer, or for any medical use. These experts further stated that the scientific literature contains no reports of adequate, well-controlled, scientific studies or other evidence upon which recognition of safety and effectiveness may be predicated. They did not know of any recognized medical text in which the use of amygdalin or any other cyanogenic glycoside is recommended for the treatment of cancer. They did not know of any medical school where use of these substances for such purpose is taught. They did not know of any expert in cancer chemotherapy who is of the view that there is evidence that these substances have any useful effect in treating cancer. They did not know of any report in the scientific literature describing an adequate, well-controlled study which demonstrates that amygdalin or any other cyanogenic glycoside is safe and effective (Dr. Daniel S. Martin, R 185; Dr. Joseph F. Ross, R 190; Dr. Charles G. Moertel, R 186; Dr. Jesse L. Steinfeld, R 194; Dr. C. Chester Stock, R 195; Dr. Harold James Wallace, R 199; Dr. Peter H. Wiernik, R 200; Dr. Emil J. Freireich, R 390; Dr. David T. Carr, R 176). The qualifications of the individuals not previously discussed are set forth in the following paragraphs:

Joseph F. Ross, M.D., is Professor of Medicine at the University of California School of Medicine at Los Angeles, California, and Director of the United States Public Health Service-funded Research Training Program in Hematology and Hematologic Oncology at UCLA. He submitted an affidavit (R 190) in which he described his educational background and experience in teaching medical students and physicians. He is actively involved in the medical care of cancer patients. Dr. Ross listed his membership in several societies and councils which deal with cancer treatment and his membership on the editorial boards of several scientific publications.

Charles G. Moertel, M.D., is Chairman of the Department of Oncology at the Mayo Clinic, Director of the Mayo Comprehensive Cancer Center, and Professor of Medicine at the Mayo Medical School, Rochester, Minnesota. He described his educational background and experience which have included serving as Editor of Cancer Yearbook, Associate Editor of Cancer Medicine, serving on the editorial board of Cancer, serving on a number of cancer committees, being involved in clinical research in pharmacology concerning cancer chemotherapy and clinical oncology, and publishing as author or co-author over 200 articles, abstracts, and editorials in recognized medical and scientific journals (R 186).

C. Chester Stock, Ph.D., is Vice President and Associate Director for Administrative and Academic Affairs of the Sloan-Kettering Institute for Cancer

Research, New York, New York, and Professor Emeritus in Biochemistry at Cornell University. He described his educational background and experience as including serving as a member of several boards and societies concerned with cancer research and serving as Chief of the Division of Experimental Chemotherapy at Sloan-Kettering, where for many years he has had a major responsibility in the development of new drugs for the treatment of cancer (R 195).

Peter H. Wiernik, M.D., is Professor of Medicine, University of Maryland School of Medicine and Chief, Clinical Oncology Branch, National Cancer Institute, Baltimore Cancer Research Center. His educational background and experiences include duties as a reviewer for 9 medical-scientific journals, co-editor of 2 journals and the author or co-author of over 140 articles, editorials, and abstracts which have appeared in medical-scientific literature most of which deal directly with cancer (R 200).

Emil J. Freireich, M.D., is Head of the Department of Developmental Therapeutics and Professor of Medicine, and Chief, Division of Oncology at the University of Texas Medical School at Houston, Texas. His educational background and experience includes membership in several societies and committees concerned directly with cancer treatment. In addition, Dr. Freireich serves as a member of editorial boards of medical and scientific journals concerned with cancer research and, as such, reviews and evaluates scientific papers relating to the causes, treatments and control of cancer. He has published in



internationally recognized journals over 250 articles, the majority of which have been concerned with cancer (R 390).

David T. Carr, M.D., is Professor of Medicine at the Mayo Medical School, Associate Director for Cancer Control and Community Relations of the Mayo Comprehensive Cancer Center, and a member of several professional societies and committees concerned with the treatment of cancer. His professional education and experience include the responsibility for a program of public education about cancer. His special interests are internal medicine and medical oncology, and he is regularly engaged in the medical management of cancer (R 176 (see also Tr. at 180-89)).

Several other experts submitted testimony in which they stated that, in their experience, Laetrile was not effective in the treatment of cancer. Their qualifications are set out in the following paragraphs:

James F. Holland, M.D., Professor and Chairman, Department of Neoplastic Diseases; Chief, Division of Medical Oncology; and Director, the Cancer Center, Mount Sinai School of Medicine, is a physician who has worked exclusively in cancer medication for over 26 years, specializing in cancer chemotherapy. He states, in his verified testimony, that he is thoroughly familiar with the action of drugs on cancer (R 396).

Carl M. Leventhal, M.D., is Deputy Director of the Bureau of Drugs, Food and Drug Administration. He holds the rank of Medical Director in the Commissioned Corps of the Public Health Service and is

Assistant Professor of Neurology and Pathology at Georgetown University. As Deputy Director of the Bureau of Drugs, he participates in meetings in which the status of Laetrile is discussed and evaluated (R 184).

William A. Nolen, M.D., is Chief of Surgery at the Meeker County Hospital, Litchfield, Minnesota. He has served on the board of editors of the Minnesota State Medical Journal and has written a number of articles, editorials, and books on subjects of public health interest, including a book entitled *Healing: A Doctor in Search of a Miracle*, in which he describes his personal experience with a patient who lost her life because she chose Laetrile for treatment of an early cancer, thereby delaying conventional medical treatment (R 138).

Thomas H. Jukes, Ph.D., is Professor of Medical Physics and Research Biochemist at the University of California, Berkeley, California. He is a member of several professional societies, serves on the editorial boards of several scientific publications, has written three books and over 250 articles in scientific journals and has conducted research in the vitamin and cancer fields (R 416 (see also R 41)).

Robert S. K. Young, M.D., Ph.D., is a physician and has a doctorate in pharmacology. He serves as adjunct Assistant Professor of Pharmacology at Georgetown University School of Medicine and Dentistry and is group leader for the Oncologic Drug Class, Bureau of Drugs, Food and Drug Administration (R 201 (see also R 430)).

(b) *Supporters of Laetrile.*—In contrast to the great amount of evidence that experts in drug evaluation do not generally recognize Laetrile (or amygdalin) as effective, the evidence in the record to the contrary is meager. The Commissioner will outline qualifications of those persons who claim any modicum of training or experience in the area of drug evaluation whose support for the use of Laetrile appears in the record. The submissions of the following three physicians are discussed under II.A.1.c. above, "The 'Evidence' of Laetrile's Effectiveness":

John A. Richardson, M.D., stated in testimony (Tr. at 462-463) that he had been in general practice for 25 years and since 1971 had been engaged in nutritional using Laetrile, amygdalin, or vitamin B-17 and that he had treated, over the past 6 years, between 4,000 and 5,000 cancer patients. Dr. Richardson made no claim to special training or board certification in the area of oncology or of training or experience in the evaluation of the safety and effectiveness of drugs. Dr. Richardson's license to practice medicine has been revoked (R 183 at 13).

Philip E. Binzel, Jr., M.D., stated that he has been a family physician since 1955 and currently serves as scientific advisor to the Committee for Freedom of Choice (Tr. Ex. 13). He stated that he has treated over 400 patients in the last 3 years with a "metabolic therapy" for cancer (Tr. at 360-361). No special training in oncology or in the evaluation of drug safety or effectiveness is claimed.

Lawrence (Larry) Patton McDonald, M.D., who stated that he has been a urologist since 1963, is a former member of the State of Georgia Medical Education Board, and is currently a member of the U.S. House of Representatives. He stated that he was a member of several societies and associations, including the American Society of Clinical Urologists, the Southeastern Section of the American Urological Association, and the American Association of Physicians and Surgeons (R 509). No showing has been made that Dr. McDonald has a specific expertise in cancer treatment or in the evaluation of the safety and effectiveness of drugs.

Dr. Edward M. Arana, who spoke at the oral argument in this proceeding, identified himself only as a practicing dentist in Carmel, California (Tr. 472-A).

Ernst T. Krebs, Jr., spoke at oral argument in this proceeding (Tr. at 228-248). While he is referred to as Doctor, he did not complete his medical training and is a doctor only by virtue of an honorary degree. No special training in the area of cancer therapy or in the evaluation of safety and effectiveness of drugs has been shown for Mr. Krebs, Jr.

Paul Hart, M.D., spoke at oral argument. He described himself as having been employed at a pathology laboratory that dealt with the effects of radiation from atomic bombing in Japan and that was associated with Deaconess Hospital in Boston (Tr. at 457-58), and as being a diplomate of the National Board of Medical Examiners (Tr. at 457). He stated

that he has an interest in "the Carl O. Simonton, M.D., psychotherapeutic approach to cancer therapy \* \* \*" (Tr. at 458). While he indicated a personal respect for various Laetrile proponents, he did not give an opinion as to whether or not Laetrile is generally recognized by experts qualified to evaluate the safety and effectiveness of drugs as safe and effective for use in cancer therapy.

Dr. Mario Soto spoke at oral argument. He described himself as being former head of the chemotherapy departments of two different Mexican hospitals. He stated that he is an independent investigator for the National Cancer Institute and a conventional oncologist and chemotherapist. He is medical director of a Laetrile clinic in Tijuana, Mexico (Tr. at 478-479).

Dean Burk, Ph.D., who spoke at oral argument and provided a written submission (R 302), is a biochemist and is president of the Dean Burk Foundation, Inc. He stated at oral argument that he had spent 50 years in research on cancer and vitamins, 35 of which were with the National Cancer Institute (Tr. at 402). His position is that Laetrile is not a drug but a vitamin.

An affidavit of Chauncey D. Leake, Ph.D., prepared for another proceeding, was submitted to this record (R 302, Ex. K). The affidavit indicates that he is Senior Lecturer in Pharmacology at the University of California School of Medicine, San Francisco. His curriculum vitae showed that he has a history of teaching, participation in organizations dealing with

medicine and pharmacology, editing of journals, and authorship of books and articles.

An affidavit of Charles Gurchot, also apparently prepared for another proceeding, was submitted as Exhibit L to R 302. His degree is in chemistry and physiology. Now semi-retired, he has taught pharmacology, biochemistry and chemistry at several schools of medicine and is a member of a number of scientific societies.

James Cason, Ph.D., submitted a statement in which he states that he has been a chemistry professor for some 35 years, has published over 100 research papers in scholarly journals and has served on the editorial boards of Organic Syntheses, and the Journal of Organic Chemistry (R 217). He is currently a professor of chemistry at the University of California, Berkeley (id.). While he states his opinion that a diet high in nitrilosides leads to a low incidence of cancer, he gives no opinion as to whether or not Laetrile (or Amygdalin) is generally recognized by qualified experts to be a safe and effective cancer drug.

The statute requires that "general recognition" be among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs (21 U.S.C. 321(p)(1)). Few of the proponents of Laetrile who have made submissions to this record possess the necessary training and experience to qualify them as such experts. The Commissioner has, however, for purposes of completeness, considered as



coming within the category of "experts" for this purpose, persons, including those listed above, who have exhibited even a small modicum of scientific experience or experience in the area in which they have offered submissions. The weight to be given the testimony of such persons, of course, must correspond to their expertise, cf. *United States v. 1,048,000 Capsules, More or Less, Etc.*, 347 F. Supp. 768, 771 (S.D. Tex. 1972), aff'd 494 F.2d 1158 (5th Cir. 1974).

The Commissioner concludes that, the lack of adequate and well-controlled clinical investigations published in the scientific literature aside, the record clearly demonstrates that the overwhelming majority of experts in the evaluation of the safety and effectiveness of drugs do not recognize Laetrile as effective. Even the proponents of Laetrile, while they may argue that the majority is wrong, could hardly be heard to argue this point. Laetrile is thus a new drug within the meaning of the act.

#### B. GENERAL RECOGNITION OF SAFETY

As noted above, for a drug to be exempt from new drug status under 21 U.S.C. 321(p)(1) it must be recognized by "experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs" to be both safe and effective under the conditions of its intended use. While lack of such recognition of Laetrile's effectiveness has already been shown, the Commissioner will discuss in addition the evidence on the question of general recog-

nition of the drug's safety. He finds that such recognition does not exist.

#### 1. Lack of Adequate Testing

As has been discussed above, for a drug to be generally recognized as safe it must have accumulated at least the amount of evidence of safety that would be required for approval of a new drug application and that evidence must be generally available to the community of experts through publication in the scientific literature. In order for a new drug application for a drug to be approved, there must exist as to that drug "adequate tests by all methods reasonably applicable" that show the drug's safety (21 U.S.C. 355(d); cf. 21 CFR 314.111(a)(1)).

An attempt to show that Laetrile had been proven by adequate testing to be safe for use in man was made in 1970 when the McNaughton Foundation submitted to FDA a notice of claimed investigational exemption for a new drug (IND) for Laetrile. The FDA terminated that exemption because of a lack of evidence of safety. Subsequent to the termination, the IND was referred to an Ad Hoc Committee of Oncology Consultants. The report of this committee is submitted with R 184 as Exhibit 2. This report states. "The Committee concurs with the action of the Commissioner in termination of IND 6734." Addressing the toxicity question, the Committee concluded (id. at 2). "Although it is often stated in the IND that amygdalin is non-toxic, data to demonstrate this

lack of toxicity are absent, particularly with respect to the oral route."

The animal studies done to show Laetrile's safety did not justify use of the dosage suggested in the IND. "[T]he sponsor wishes to begin oral studies in patients at 2.95 mg/kg (oral); this is to be compared with a documented safe oral dose in dogs of 7.5 mg/kg daily for 6 months \* \* \*. On the basis of documented data, if substantiated, then a proper starting dose that might be considered in man, would be 1/10 of 7.5 mg/kg or 0.75 mg/kg (oral). The proposed starting dose of 2.95 mg/kg is 1/100 of the oral acute LD in mice. It is considered to be dangerous to base the starting dose for a chronic (6 + weeks) study in man on a single dose study in mice. It is also dangerous to initiate human studies while the nature of the toxicity has not been elucidated in large animal species. No documented data are presented in the IND to permit a higher starting dose" (id. at 3-4).

Dr. W. Sherwood Lawrence, Executive Secretary for the State of California Cancer Advisory Council states (R 183 at 17), "An extensive review of the world's scientific literature has been made by the Council. The evidence available for the determination of the recognition of safety of the compound is characterized by the lack of a body of scientifically sound information such that experts qualified by experience and training to make such determinations are unable to do so. In the absence of such a determination by

qualified experts Laetrile (amygdalin) cannot be considered to be generally recognized as safe."

There is thus an absence of scientifically sound data upon which experts qualified by training and experience to evaluate the safety and effectiveness of drugs could base an opinion that Laetrile is safe for use in man. In the absence of such data the Commissioner must conclude that the safety of use of Laetrile in man has never been, and is not now, "generally recognized" by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs.

## 2. *Testimony of Experts*

The Commissioner's conclusion of lack of general recognition among experts of Laetrile's safety is supported by testimony of such experts in the administrative record. (The qualifications of the experts whose statements are quoted have been discussed above.)

As one expert notes, while the toxicity of injected Laetrile has not been studied, there is evidence that amygdalin when ingested (eaten) is harmful to humans, evidence that has led to cautions on the part of Laetrile promoters themselves: In discussing the use of Laetriles, Dr. W. Sherwood Lawrence states (R 183 at 16), "There has never been a formal evaluation of the safety of these compounds to determine their safety. Although the proponents claim Laetriles are non-toxic, there are bonafide reports of clinical toxicity on oral intake (California Morbidity Reports,

Ankara), and even fatality (Bitter Almond Poisoning, Zmedizinfrul). Furthermore the proponents themselves are aware of this toxicity as evidence by the proposed labeling submitted in an application for an exemption for an Investigational New Drug which warned: "CAUTION: Laetrile is not to be taken orally. It is extremely toxic by this route of administration \* \* \*.' There are not studies adequately showing the distribution, activity and metabolic fate of the parenterally administered compound. Chronic effects are not studied and reported in depth. There is cause for the concern as other similar beta-cyanogenetic compounds cause serious toxic effects when ingested on a chronic basis, e.g., Tropical Ataxic Neuropathy in Nigeria (Attachment 20). Effects of industrial poisoning from chronic low concentration exposure are well-known." (See also, for discussion of toxicity of Laetrile, section V.B.3. below. "Dangers of Ingestion of 'Vitamin B-17'".)

Dr. Robert C. Eyerly reports, "One of the unproven remedies for cancer management which the committee (on Unproven Methods of Cancer Management) investigated is the drug Laetrile. Other names for Laetrile include amygdalin and prunasin. These compounds are classified as cyanogenic glycosides. Cyanogenic glycosides, including amygdalin, are generally regarded as toxic substances, rather than as foods, because when they break down they liberate hydrogen cyanide, one of the most toxic substances known" (R 167 at ¶ 8).

Dr. Robert S. K. Young states (R 430 at ¶¶ 4, 5, and 7), "The FDA does not have authenticated or

validated data on the toxicity of amygdalin in humans. It does not have scientific studies or the data upon which scientific studies might be constructed, in humans receiving amygdalin which would allow it to define the toxic effects of this drug. There are no such reports in the medical literature. Nevertheless, Dr. Nepier from Germany has reported that amygdalin causes hypotension and hemoglobinurea in humans. There have been reported cases of cyanide poisoning in humans who ate apricot kernels. The symptomatology includes dyspnea, cyanosis, vomiting, prostration, convulsions, stupor, and paralysis. Since these toxic effects are caused by the cyanide, which is a constituent part of amygdalin, amygdalin could cause the same toxic effects. Although it is possible that amygdalin can be given to humans in doses which are non-toxic in man, the drug is unsafe for use in humans. There is no scientific evidence that the drug can cure or is effective as a treatment for any human cancer." Dr. Young also states (id. at ¶¶ 2-3), "There is a difference between a drug's toxicity and a drug's safety. The toxic effects of a drug are those effects which are not beneficial to the person taking the drug, but are deleterious. The safety of a drug is defined by the context of its use and includes consideration of issues such as a disease for which the drug is intended, the alternative remedies which are available and their efficacy and safety, and the possible abuse of the drug by those who do not have the disease for which the drug is intended. Acute toxicity tests of amygdalin have been carried out in animals.



It appears that relatively large quantities of amygdalin can be given parenterally. When given by the oral route, however, the toxicity of amygdalin is greatly increased (by a factor of approximately twenty-five times)."

James F. Holland, M.D., indicated that he does not accept the theory of proponents of Laetrile that patients should be allowed to take Laetrile since, even if it is ineffective, it cannot hurt. He states (R 396 at 1), "It can hurt by interfering with patients' acceptance of indicated therapy in the mistaken and false hope of potential benefit from Laetrile. Delayed operation, refused radiotherapy, skipped chemotherapy all risk an increasing cancer morbidity and mortality because of the premise that Laetrile is active. This is a very dangerous side effect, indeed."

In addressing whether or not Laetrile is safe, Dr. Carl M. Leventhal states (R 184 at ¶ 19), "The question of whether Laetrile is now, or ever was, generally recognized as safe goes beyond the absence of any evidence indicating the lack of toxicity of the drug. The safety of a drug for human use depends, in large measure, on the therapeutic effectiveness of the particular drug. When patients forego effective forms of therapy and turn instead to worthless potions and nostrums, their disease may progress while effective therapies are forsaken. In the case of cancer, treatment with an ineffective drug will inevitably and inexorably lead to the patient's death. Seen in this light, an ineffective cancer drug is inherently unsafe and even lethal, because of the patient deaths which will necessarily ensue."

Dr. Harold J. Wallace, Jr., states (Tr. at 174) that: "The safety of the various forms of amygdalin has not been tested by the usual scientific methods of clinical pharmacology. There is evidence that the crude oral form can and has caused toxicity in humans and may cause death. There has been no documentation of the usual parameters that we require of drugs when used in a clinical situation. We don't have blood levels achieved, activation clearance, metabolism, distribution or excretion of amygdalin compounds in man, as is usually required in the pre-clinical and clinical evaluation testing of chemotherapeutic compounds or other drugs."

Dr. Frank Rauscher, a former Director of the National Cancer Institute (NCI), and currently associated with the American Cancer Society, said in his statement concerning Laetrile, while he was Director, NCI: "Assertions of the non-toxic nature of Laetrile have not been demonstrated in vigorous clinical studies. Even if this claim is true, there is no basis whatsoever for recommending the clinical use of any non-toxic agent if it cannot be expected to produce objective clinical benefits" (R 173, Att. "Statement Concerning Laetrile" at 2-3).

Dr. Thomas H. Jukes states (R 41 at 1): "Laetrile is not generally recognized by experts as safe. In the presence of the enzyme beta-glucosidase, Laetrile is hydrolyzed to glucose and mandelonitrile. Mandelonitrile readily decomposes with the liberation of hydrocyanic acid, which is extremely poisonous at low levels. The enzyme beta-glucosidase is widely

distributed in materials of plant origin. The potential danger that laetrile may be decomposed with liberation of hydrocyanic acid makes it unsafe."

Dr. George J. Hill, II, after noting that ineffective remedies for cancer can lead to delay in treatment and "needless and untimely death," states: "In the absence of scientific evidence of effectiveness, no drug intended for use in treating cancer can be regarded as safe" (R 170 at ¶ 11).

Dr. Joseph F. Ross noted that that delay in cancer therapy because of use of Laetrile "results in loss of life, tragic suffering, and shortened life span" (R 190 at 8) and that use of the drug is "hazardous to the health of cancer patients" (id. at 7). He states: "Additionally, the use of 'Laetrile,' Vitamin B-17, 'Aprikern' and other such amygdalin containing materials when ingested presents a definite health hazard. The action of gastrointestinal fluids and enzymes releases the C=N (cyanide) radical from the compound and this may produce acute cyanide poisoning" (id. at 8).

Several additional experts submitted affidavits in which they state that neither amygdalin nor any other cyanogenic glycoside has ever been generally recognized as safe (Dr. Charles G. Moertel, R 186 at ¶ 12, Dr. Jesse L. Steinfeld, R 194 at 5-6; Dr. Peter G. Wiernik, R 200 at ¶ 16; Dr. Emil J. Freireich, R 390 at ¶ 19; and others).

### III. THE "GRANDFATHER" ISSUE

Because Laetrile is not generally recognized by qualified experts as safe and effective (see discussion above), it is subject to the Act as a "new drug" unless it is exempted from the statute's provisions under either of the two "grandfather clauses." These two exceptions, described in more detail below, limit the protection provided to the public with respect to certain drugs that fulfill a number of carefully defined conditions. Accordingly, the courts have recognized the narrowness of the exceptions. *United States v. Allan Drug Corp.*, 357 F.2d 713, 718 (10th Cir. 1966) cert. denied 385 U.S. 899 (1966): "Since we are dealing with a Grandfather Clause exception, we must construe it strictly against one who invokes it."; *Durovic v. Richardson*, *supra*, 479 F.2d at 250 n. 6; *United States v. An Article of Drug \* \* \** "*Bentex Ulcerine*" \* \* \*, 469 F.2d 875, 878 (5th Cir. 1972), cert. denied 412 U.S. 938 (1973); *United States v. 1,048,000 Capsules, More or Less, Etc.*, *supra*, 347 F.Supp. at 770.

The Court in *Bentex Ulcerine* held, 469 F.2d at 878, that any party seeking to show that a drug comes within the grandfather exemptions "must prove every essential fact necessary for invocation of the exemption." Accordingly, the Commission concludes that Laetrile will not qualify for grandfather clause exemption unless each of the essential facts has been proved by evidence submitted in the record.

In the February 18, 1977 FEDERAL REGISTER notice initiating this proceeding, proponents of Laetrile were informed of their obligation to bring forth evidence that would support their claim that Laetrile qualifies for this exception. The notice set forth the provisions of a regulation (21 CFR 314.200(e)(2)) that detailed the format to which submissions directed to the grandfather clause exceptions should conform (42 FR 10069). Failure to submit formulas, labeling and evidence of marketing in that format was stated to constitute a waiver of any contention that Laetrile was exempt from new drug provisions of the act. Failure to submit evidence in the format has resulted in such a waiver.

Despite the waiver, the Commissioner, in order to fully address the issue remanded by the courts, has culled the entire record for evidence that might arguably be relevant to the grandfather status of Laetrile. He has considered this evidence in determining whether the essential facts necessary to invoke the grandfather clause exemptions have been proved. Moreover, against the chance that it should later be held that those contending that Laetrile's use is illegal must prove the nonexistence of the essential facts necessary for the invocation of the grandfather clause exceptions, the Commissioner has considered the evidence in the record in light of this possibility.

The essential facts necessary to invoke the two exemptions are discussed, together with the evidence relevant to each, below. The Commissioner's con-

clusions on these issues may be summarized as follows:

(1) Contentions that Laetrile qualifies for either grandfather clause exception are waived.

(2) Evidence presented does not prove the existence of each essential fact necessary to the invocation of either grandfather clause.

(3) While it is of course not possible to prove a negative with regard to the existence of each of the essential facts involved, the record assembled contains substantial evidence, constituting a clear preponderance of the evidence submitted, that these essential facts do not exist.

#### A. THE 1938 GRANDFATHER CLAUSE

To qualify for exemption from the definition of a new drug under the 1938 grandfather clause, it must be shown that the drug "at any time prior to the enactment of this chapter [1938] \* \* \* was subject to the Food and Drugs Act of June 30, 1906, as amended, and \* \* \* at such time its labeling contained the same representations concerning the conditions of its use; \* \* \*" 21 U.S.C. 321(p)(1).

Thus, to qualify for this exemption, it must be proved that (1) the identical drug (2) bearing labeling containing the identical representations concerning the conditions of its use (3) was introduced into interstate commerce in the United States (or was manufactured in a Federal territory or the District of Columbia) after June 30, 1906 and prior to the enactment of the act in 1938. The



exemption applies only to drugs whose labeling with respect to representations as to conditions of use has undergone no changes whatsoever from the labeling utilized prior to the passage of the 1938 act, and whose composition is completely identical to its composition prior to this passage. If any change in representations for conditions of use in labeling or any change in composition has occurred since the enactment of the 1938 act, such change precludes the applicability of the 1938 exemption. The proof required would necessarily involve the production of quantitative formulas, labeling, and evidence of marketing both for the pre-1938 use and for the present use. While submissions to the administrative record contained a number of references to use of Laetrile or its predecessors before 1938, no proof was submitted to show that what was termed "Laetrile" or "amygdalin" as used before 1938 was the same drug which is now being marketed. Nor is there any indication whatever that the labeling of the various drugs claimed to have been marketed before 1938 contained representations concerning conditions of use which are identical to the representations associated with the presently marketed drug. It should be noted that the term "labeling" is defined in the act to include not only "all labels" but also, "other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article," 21 U.S.C. 321(m). This definition has been given a broad interpretation, see, e.g., *Kordel v.*

*United States*, 335 U.S. 345, 347-50 (1948); *United States v. Urbutcit*, 335 U.S. 355, 357 (1948).

A number of submissions in the record referred to use of substances claimed to be related to Laetrile or amygdalin in ancient times. While each of these statements was hearsay unsupported by any sort of corroborating evidence and thus cannot be considered trustworthy, it is apparent that even if accepted at face value these claims would not justify invocation of the 1938 grandfather clause. Examples of such claims in the record include those found in a McNaughton Foundation article entitled "Information for Physicians: Amygdalin, The Non-Toxic Analgesic" which cites use by the Chinese 3,500 years ago as well as use by the Greeks and the Romans (R 183, Att. 106 at ¶ 1). See also *Hanson v. United States*, 417 F.Supp. 30, 36 (D. Minn.), aff'd 540 F.2d 947 (8th Cir. 1976) (copy of opinion attached to R 173), noting that plaintiffs in that court action had introduced hearsay concerning the use of amygdalin by ancient Egyptians, evidence upon which the court did not rely; affidavit of Chauncey Leake, Ph.D.—recommendation of almonds for various purposes (not to cure cancer) by a first century Greek surgeon (R 302 Ex. K); statement by John J. O'Connor, Jr., in support of a Maryland State bill on Laetrile—bitter almond used by Chinese for the treatment of tumors 3,500 years ago; use by Greeks and by Romans (Tr. Ex. 4, Att. at 22).

Other submissions mentioned that amygdalin was prepared by two Frenchmen in 1830 and analyzed by

two Germans shortly thereafter. (See R 183, Att. 10b at ¶ 1; R 302, Ex. K; R 168, Att. at 345; R. 80, Att.) No claims were made that these 19th century experimenters used amygdalin to treat cancer. There is a claim, however, that a Russian physician used amygdalin for that purpose in 1845. The reference is to a report in the *Gazette Medicale De Paris*, Tome XIII, Samedi, Le 13 Septembre 1845, by Dr. Inosemtzeff. This article is referred to in a number of submissions. (See, e.g., R 259, Att. at 1.) It was not, however, itself submitted and in thus not part of the record available for analysis by the Commissioner. According to the description in the "Listing of Documents Relative to \* \* \* Laetrile" attached to R 259, a submission by Mr. Wynn Earl Westover, the author of the 1845 article was a professor of surgery at the Imperial University of Moscow, and his article described two cases of cancer apparently successfully controlled for 11 years and 3 years, respectively, by the use of amygdalin (for other references to this article, see R 260, Att. at 1; R 302, Ex. L at ¶ 5).

As is obvious, this "evidence" relating to ancient and 19th century use is irrelevant to the 1938 grandfather clause issued for the following reasons: (1) It does not indicate that the drug was used in the United States after June 30, 1906 and before 1938. (2) It gives no indication that the drug used was the same as Laetrile. Most of the references in fact indicate that the substances used were either some extract of almonds, or, as in the case of the alleged Russian physician, simple amygdalin, (3) no suggestion that

any drug was to be used in accordance with the indications now associated with treatment with Laetrile may be found in these references. Again, where the submissions go into detail concerning the historical uses of almonds or amygdalin, it is apparent that different conditions of use are involved.

A number of claims purporting to be relevant to the 1938 grandfather issue dealt with the appearance of almond extract in various Pharmacopeia, (See, e.g., Tr. at 250; R 302, Ex. K and Ex. L, ¶ 9-12 Tr. Ex. 9.) The opinion in *Hanson v. United States*, *supra*, indicates that plaintiffs in that case relied upon a listing of amygdalin in the Merck Index of 1896. The references in the Pharmacopeia involve in each case some sort of almond extract. There is no indication that that extract was to be used as an injection to cure, control, or prevent cancer. The references to the Pharmacopeia, as is the case with other general, unsupported references indicating use in cancer patients in previous centuries (see, e.g., R 509 at 2) are for the reasons detailed simply not probative of grandfather status.

Of more direct relevance to possible grandfather status is the information in the record regarding the work done with what was apparently Laetrile's predecessor by Dr. Ernst Krebs, Sr. A great deal of conflicting information regarding the dates of Dr. Krebs' work was submitted to the record. There are numerous instances in the record of statements that Dr. Krebs developed a drug related in some way to modern day Laetrile either in 1920 or shortly thereafter,

while a new and allegedly nontoxic form of Laetrile was developed by Ernst T. Krebs, Jr., in 1952 or in the early 1950's. See e.g., the American Cancer Society Committee on Unproven Methods of Cancer Management's article on Laetrile (R 167, Ex. 2); A Report on the Treatment of Cancer with Beta-Cyanogenetic Glucosides ("Laetriles") by the Cancer Advisory Council, State of California (1963) at 2 (R 183, Att. 16). The latter report may be the genesis of the 1920 date, though the former indicates that it is reporting the date "According to" Dr. Krebs. At any rate, the 1920 date appears in or is alluded to in a number of submissions (see R 173, Att., "Questions Most Frequently Asked," and Att., "Laetrile: The Making of a Myth," FDA Consumer (Dec. 1976-Jan. 1977) at 6; R 184 at ¶ 6; Tr. at 272; Tr. at 41; R 250 at 2-3; R 170, Ex. 3 at 2104; R 258, Ex. 16; R 386; Tr. Ex. 10; R 183, Ex. 3 at 33). There may have been some basis for the original statement that Dr. Krebs had begun to work or had achieved results on a substance containing amygdalin in 1920 or in the early 1920's, but nothing has been submitted to indicate what that basis is. The apparent manner in which one submission has relied upon another on this question illustrates the undesirability of relying on hearsay accounts to prove a fact of this kind. None of these statements indicate, in any case, that the materials with which Dr. Krebs was experimenting were identical to, and were used under conditions indicated in labeling which were identical to, the composition and indications for present day Laetrile.

Michael L. Culbert, representing the Committee for Freedom of Choice in Cancer Therapy at the oral hearing, stated: "Dr. Krebs, Sr., both publicly and privately and in numerous different ways, has published not only results but some labels of material that goes back to the 1920's when Dr. Stohl in Switzerland and a number of Japanese scientists and Dr. Krebs, Sr., and others were working with the original extract" (Tr. at 41). If Mr. Culbert or his group have in their possession such publications, they have not submitted them.

A document submitted which would seem, questions of credibility aside, to be the most reliable on the question of the dates of Dr. Krebs' work and that of his son is an affidavit signed and sworn to by Dr. Krebs on April 28, 1965. This affidavit, taken by an FDA employee, appears as Exhibit 6 to R 184 and as attachment 13 to R 183. Since this affidavit is under oath and is by the person most likely to know of the dates in question, the Commissioner concludes that where the dates in the affidavit are different from those appearing elsewhere, chief reliance should be placed on the affidavit. In the relevant paragraphs, Dr. Krebs says:

\* \* \* \* \*

2. In 1926, I made an extract from apricot kernels which I called Sarcarcinase. This extract contained Amygdalin and 1-glucosidase. When I injected this product into rats it was toxic and killed some of them.

3. In 1936, I changed the composition of the preparation resulting from the extract of apri-



cot kernels so that the only active principle which remained was Amygdalin.

4. During the period between 1936 and 1960, I perfected the purification process so that the purity of the Amygdalin rose from 66 percent in 1936 to 99.8 percent by 1960.

5. In 1955, I began to lyophilize the Amygdalin and I have been lyophilizing it in its final form ever since when I produce it in my laboratories.

6. In 1949, my son, Ernst T. Krebs, Jr., gave the name Laetrile to the Amygdalin I was producing and I have used the name of Laetrile ever since that time for the final form of the Amygdalin which I produce.

7. As early as 1926 and up through 1962, I first began to ship and have done so continuously thereafter the Sarcarcinase extract (cf 2), then the amygdalin (cf 3), then the purified amygdalin (cf 4), then the purified and lyophilized amygdalin (5), and then since 1949 (cf 6) the latter under the name of Laetrile to persons in other States outside of the State of California and in many other countries. Many of these persons have reported their studies in scientific and medical journals and in private communications over several decades. The above shipments were for investigational use only.

As the dates cited by Dr. Krebs illustrate, the substance with which he experimented in the 1920's and 1930's was not the same substance as that which he was using in 1962. The pre-1938 use is, for that reason alone, not sufficient to qualify Laetrile for

exemption from coverage of the act under the 1938 grandfather clause.

In another document upon which the Commissioner would ordinarily place reliance, a December 15, 1962 [sic] report by FDA inspectors describing their conversations with Dr. Krebs, Sr. (R 184, Ex. 5), Dr. Krebs is reported to have stated that "he began experimenting some 10 months ago with the extraction of Cyanogentic Glucoside from a mixture containing apricot pits. The purification of this glucoside was effected in the laboratories of Dr. Krebs and used in the treatment of his patients with, according to him, satisfactory results. This material assertedly liquefies malignant growths by the release of cyanide in the area. Injections are made around the area and the case of lung cancer injections are made in the apex of the trapezei." It may be that Dr. Krebs in his statement to the inspectors was speaking of his efforts to purify Amygdalin, referred to in paragraph 4 of his affidavit. On the second page of the inspectors' report, they indicate that "E. T. Krebs, Jr., stated that Dr. Harry Pincus Jacobson, M.D., was the first to use 'Laetrile' on humans and that this was in June 1952. Up to the present time (December 1952) he has used the product on approximately 14 cases."

This last quotation from the inspection report comports with statements elsewhere indicating that in 1952 Mr. Krebs, Jr., developed a new product, related to the products with which his father had been working, which he called Laetrile. While the failure of the affidavit of Dr. Krebs, Sr., to mention this "im-

provement" by Mr. Krebs, Jr., might lead one to question whether such an improvement had taken place, an article by the senior Krebs and Dr. Arthur Harris, copyright 1955, entitled, "The Treatment of Breast Cancer with Laetrile by Iontophoresis" (R 183, Att. 7) at 23-24, states as follows:

In 1952 the senior author's biochemist son, Ernst T. Krebs, Jr., became interested in the preparation his father had used on cancer for so many years. In his laboratory—the John Beard Memorial Foundation—he tore the drug apart and came to the conclusion that it was not only the glucoside but more particularly the cyanogenetic glucoside that had benefited cancer patients. He succeeded in separating the enzyme Emulsin from the cyanogenetic glucoside and advised their administration separately, in order to avoid the premature trigger-off of HCN from the chemical breakdown in the somatic (or normal) tissue, for this gas—HCN—was the active agent in destroying the cancer cell.

Again the senior author tried each purified preparation—the cyanogenetic glucoside and the enzyme Beta-glucosidase—separately. He administered the cyanogenetic glucoside parenterally (by injection) and followed it in fifteen minutes or so with an injection of the enzyme Beta-glucosidase. The cancer victims so treated tolerated both the drug and the enzyme excellently—and were immeasurably improved. Using the chemical and the enzyme separately, therefore, gave a high degree of safety as well as enhancing its cancerolytic effect.

\* \* \* \* \*

Because this apricot kernel preparation was "Laevorotatory" (left-handed) to polarized light, and because Amygdalin was chemically a "mandelonitrile," Krebs, Jr., united the first and last syllables to invent a name for the new cancericidal drug—LAETRILE.

Krebs Jr. uncovered the vital link that united Laetrile with the Unitarian or Trophoblastic Thesis of Cancer. In the previous chapter we emphasized the known fact that most malignant lesions are focally characterized by high concentrations of the enzyme Beta-glucuronidase—one of the main attributes common to both the trophoblast cell and the cancer cell. The Beta-glucuronidase of the animal kingdom is the equivalent of Emulsin in the vegetable kingdom, and Emulsin is the very enzyme that Krebs, Jr. separated from Amygdalin to make the empirical apricot formula safe for parenteral (injection) administration to humans!

This was an epochal milestone. Krebs, Jr., worked and experimented feverishly now; he was on the brink of cataclysmic discoveries, discoveries which, if substantiated, could mean victory over invincible Cancer!

He found that when he added Emulsin to Laetrile and incubated the mixture, hydrocyanic acid gas (HCN), one of the deadliest of gaseous poisons, was given off. He found that when he added animal Beta-glucuronidase (or prepared enzyme Beta-glucosidase) to Laetrile and incubated the mixture, HCN was again given off. This, he knew then, was the reaction that took place within the body—IN THE CANCER CELL!

The need for Krebs, Jr.'s improvement was related to the lack of safety of his father's original preparation. As this article co-authored by the senior Krebs states, the original "preparation proved so toxic that he and his colleagues who were experimenting with him were reluctant to continue its use, except in dire circumstances" (id. at 23; cf R 167, Ex. 2; R 170, Ex. 3 at 2014; R 386, Att. at 2-3). Again, it is apparent that the improvement in the substance used by the Krebs (father and son) after 1938 made the drug different in composition, and also in indications for use, from the drug which was used before 1938. The 1952 date appears at several points in the record. (See e.g., R 167, Ex. 2; R 173, Att. "Laetrile: The Making of A Myth" supra; R 173, Att. 3; R 184 at ¶ 6; R 189; Tr. at 272; R 250 at 2-3; Tr. Ex. 10 at 3.)

In the submission of Mr. Wynn Earl Westover (R 259) (see also R 260), in a document entitled "Listing of Documents Relative to the Krebs Enzyme Extracts Later Known as Laetrile," at 13, there is a list of registrations of trademarks and issuances of letters patent allegedly granted for Sarcocarpinase during the years 1930 through 1935. These documents have not all been submitted. Apparently submitted as representative of the patents is a patent specification from the Government of Ireland. As the above discussion indicates, the material covered in these patents is different from the material now known as Laetrile. A submission by Eric E. Conn, Professor of Biochemistry at the University of California,

Davis (R 424) discusses this patent application and states that if the procedure set out in the patent is followed, "much or all of the amygdalin in the intact kernels may be destroyed by enzymes set in action by the grinding" of the kernels to produce the extract. Most of the amygdalin remaining would be lost in processing. The extract produced "would be a mixture of glycerides, esters, certain pigments and other fat-soluble compounds that might or might not also contain a small amount (less than 5 percent) of the amygdalin remaining in the finely ground kernels." Compare the claims by Robert W. Bradford, President of the Committee for Freedom of Choice in Cancer Therapy, Inc., at the oral argument, that "Laetrile was first offered for sale in a trademark assigned in 1934, that it was sold at that time in three different forms: tablets, capsules, and injectables, (and that it) pharmaceutically was the same substance used today in cancer therapy. There can be no disagreement on this point" (Tr. at 346). Mr. Bradford submitted nothing to support his claim, which is at odds with the factual information submitted in the record and discussed above.

The Westover submission (R 259) also includes copies of a number of letters by various doctors who indicate that they have used the senior Krebs' formulation in the treatment of tumors or cancer. The letters bear dates in the 1930's, Mr. Westover's submission claims that there are a large number of other letters, not submitted, which are of generally the same type. Ernst T. Krebs, Jr., appearing at the



oral argument, testified that amygdalin had been used as early as 1932. He indicated that the product then in use was labeled Sarcarcinase. (See Tr. at 232, 238, 246.) Sarcarcinase is the name of the product which was, according to Mr. Westover, granted a United States trademark in 1934. (See also Tr. at 446-48.) Two affidavits, apparently prepared for some court action, by Charles Gurchot, Ph.D., and Chauncey Leake, Ph.D., indicate that the affiants were involved in the treatment of patients with Krebs, Sr.'s product in the 1930's (R 302, Ex. K and L).

The Commissioner has carefully surveyed the entire administrative record brought together for this proceeding. While it appears that Dr. Krebs, Sr., was utilizing some substance, which apparently had the trademark name of Sarcarcinase, before 1938, there is no evidence that that substance is identical in its formulation, or in its indications for use, to present day Laetrile (cf R 416 at ¶ 27(I)(7) (pg. 23)). In fact, as discussed above, the record is clear that the substance with which Dr. Krebs, Sr., experimented in the 1930's is different from the drug now being used by Laetrile proponents. The evidence suggests that the substance used by Dr. Krebs, Sr., in the 1930's was too toxic for general use. This toxicity appears to have been the reason for the work of Mr. Krebs, Jr., which, apparently, culminated in a substantial change in the formulation around 1952.

The Commissioner thus concludes that (1) no proof has been offered which shows that Laetrile was used and labeled before 1938 in a manner identical to its

present use and labeling, and that (2) the evidence in the record demonstrates that present day Laetrile was not developed until after 1938. Thus, regardless of where the burden of proof lies in an administrative proceeding of this type, the Commissioner must conclude that Laetrile is not eligible for exemption from the protection to the public provided by the new drug provisions of the act because of use prior to 1938 involving identical labeling as to conditions of use.

#### B. THE 1962 GRANDFATHER CLAUSE

The provision that has been characterized as the "1962 grandfather clause" is set forth at section 107(c)(4) of Pub. L. 87-781 (note following 21 U.S.C. 321):

(4) In the case of any drug which, on [October 9, 1962] the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective application under section 505 of the Act, the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

The "basic Act as then in force" read in relevant part as follows:

Sect. 201. For the purposes of this Act—

\* \* \* \* \*

(p) The term “new drug” means—

(1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a “new drug” if at any time prior to the enactment of this Act it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug the composition of which is such that such drug, as a result of investigations to determine its safety for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

The Commissioner has previously admitted that one of the conditions for 1962 grandfather status does exist—Laetrile (or amygdalin) was not covered by an effective NDA on October 9, 1962. (See 42 FR 10069). The Commissioner concludes on the basis of the information in the administrative record that Laetrile (or amygdalin) fails to meet all of the other requirements for qualifying for the 1962 grandfather clause exemption: (1) No showing has been made that a drug was used or sold on October 9, 1962 which has the same composition as a drug used or sold, or

sought to be used or sold, today. (2) The record is clear that any use of drugs called “Laetrile” or “amygdalin” in cancer therapy in 1962 was for investigational use. Investigational use can not provide the basis for exemption from new drug status on October 9, 1962 (see section 201(p)(2) of the act as then in force, set forth above) and of course does not constitute commercial use or sale. (3) No showing has been made that conditions of use recommended in labeling of a drug used or sold on October 9, 1962 are the same as those now recommended in labeling for the same drug. In fact, neither present labeling nor labeling in use on October 9, 1962 has been submitted to the record. Review of labeling available for “Laetrile” before and after October 9, 1962 reveals substantial changes in the prescribed conditions of use. (4) Laetrile (or amygdalin) was not generally recognized, by experts qualified by scientific training and experience to evaluate drug safety, as safe for use in cancer therapy on October 9, 1962.

As has been noted above, the Commissioner has concluded that the proponents of the proposition that Laetrile is exempt from the act because of “grandfather” status must bear the burden of proving that it is exempt. As has also been previously noted, however, the Commissioner has made a determination based on the alternative theory that the Government must prove that at least one of the essential facts leading to exemption does not exist. Proof of a negative is obviously more feasible in some instances than

in others. The record leaves no doubt that use of Laetrile (or amygdalin) on October 9, 1962 was for investigational purposes and that use of the drug in cancer therapy was not "generally recognized" by qualified experts to be safe on that date. Since neither the present composition nor the present labeling of the drug appears in the record, it may not be conclusively determined that the composition and the conditions of use suggested in that labeling are not the same as the composition and suggested conditions of use of some drug in 1962. Nonetheless, the Commissioner is able to conclude, based upon substantial evidence which constitutes the preponderance of the evidence in the record, that neither of those essential facts (i.e., identical formulation and identical conditions of use) do exist as to Laetrile (or amygdalin).

### 1. Composition

Clearly, for the 1962 grandfather clause to apply, the identical drug must have been used or sold in 1962 as is presently used or sold. The fact that a drug with the identical name (or names) was being used is irrelevant. Similarly, the fact that a drug in commercial use on October 9, 1962 has ingredients (such as amygdalin) in common with drugs in use today would not be sufficient under the grandfather clause if any of the ingredients of the drug, or the proportions in which those ingredients appeared in the drug, had changed (see generally 21 CFR 310.3 (h)). Even a change in an inactive ingredient will

make a drug a "new drug," (see 21 CFR 310.3 (h)(1); *United States v. Article of Drug "Entrol-C Medicated,"* 513 F.2d 1127, 1130 n. 7 (9th Cir. 1975)).

The discussion earlier in this opinion of the identity of drugs characterized at different times as "amygdalin" or as "Laetrile" illustrates the wide variation in composition of these drugs. There is no evidence in the record of the present formulation of Laetrile or of amygdalin medication. Neither is there evidence of the composition of such a drug on October 9, 1962. The Commissioner thus concludes that there has been no showing that Laetrile or amygdalin as presently constituted was in use on October 9, 1962. The Commissioner also concludes, based upon the evidence of wide variation in the drugs' composition, both before and after 1962 (discussed below), that the 1962 versions and the versions of the drugs currently in use are not identical.

It should be noted that the Commissioner's decision on this point is in accord with a statement by Andrew McNaughton of the pro-Laetrile McNaughton Foundation, discussed earlier, that data on Laetrile obtained prior to 1968 are frequently not reliable because of the variability in composition of early preparations (R 173, Att., "Report of Ad Hoc Committee of Oncology Consultants"). Other evidence on the question of composition of the drugs consists of (1) analyses done of Laetrile products and (2) representations made as to the products' composition. (The



discussion of the 1938 grandfather issue sufficiently catalogues and disposes of claims that drugs similar to Laetrile or amygdalin were marketed prior to 1938, and this section will thus discuss evidence post-dating 1938.)

*Analyses.* As discussed previously, the results of analyses of drugs called "Laetrile" have often been at variance with their labeled composition. Analyses by Canadian investigators, reported in 1965, found that two versions of the drug, one manufactured in the United States and one manufactured in Canada, had different compositions. The American version contained  $98 \pm 2$  percent amygdalin plus .5 percent phenol. The Canadian version contained  $87 \pm 2$  percent amygdalin, 5 percent di-isopropylammonium iodide, and  $8 \pm 2$  percent sucrose (R 189, Att., "Laetrile: A Study of its Physiochemical and Biochemical Properties" at 1059).

Analyses done in 1961 and 1962 for the California Cancer Advisory Council of samples of Laetrile from various different sources—samples obtained in 1951 and 1953, samples obtained from Hale Laboratories, and samples obtained from Dr. Krebs, Sr.—also showed a variation in composition among the drugs (R 183, Att. 16 at 27). Similarities to commercial amygdalin were revealed in some tests. (See, e.g., R 183, Att. 16 at 28 and App. 8.) "The old Laetrile (1951 and 1953) was similar but not identical to amygdalin in the (infra-red examination), while the new Laetrile exhibited certain similarities and cer-

tain dissimilarities to both the old Laetrile and to amygdalin" (R 183, Att. 16, App. 8 at 1). Some samples were found to contain inorganic iodine; others did not contain that substance. (See, generally, R 183, Att. 16, App. 7 and 8.)

*Claims.* A new drug application submitted to FDA by Ernst T. Krebs, Jr., on October 3, 1962, lists the composition of Laetrile as:

L-mandelonitrite-diglucoside [amygdalin] 1,000 mg.  
N, N-diisopropylammonium iodide 50 mg.  
Inactive saccharides, principally sucrose 176-250 mg.

The drug was to be reconstituted with a sterile isotonic solution (R 201, Ex. B at 101-102).

Dr. Krebs, Sr., in his 1965 affidavit, stated that his preparation contained amygdalin as its only active principle and that that amygdalin, by 1960 at least, was lyophilized and 99.8 percent pure. (See R 183, Att. 13.) It is not clear whether other, inactive, ingredients were a part of the drug he prepared.

A 1953 letter from Ernst T. Krebs, Jr., to California medical authorities states that he was forwarding to Dr. Macdonald "samples of biosynthetically degraded amygdalin in which one dextrose was removed by prunasin and the resulting compound, in the presence of platinum black, was oxidized to the corresponding glucuronoside" (R 183, Att. 14).

In 1965, FDA investigators obtained examples of labeling utilized by the senior Krebs' laboratory. The

labeling indicates that Laetrile is "cyanide glucoside type amygdalin." Additional labeling, a pamphlet entitled "Laetrile: Directions for the Administration of Laetrile," states that the drug is to be reconstituted with water, a non-isotonic solution (see R 201 at ¶ 10a and Ex. C).

Mr. Krebs, Jr., in a 1970 article in the Journal of Applied Nutrition (R 183, Att. 10c) in which he explained his theory that Laetrile and similar substances make up Vitamin B-17, suggested the drug use of a substance clearly different from all other Laetrile drugs previously in use. While what had been used previously had apparently been a manufactured drug containing either the "Laetrile" of his own formulation or amygdalin in a more or less purified form, in this article he advised that "one gram of defatted apricot seed or kernel carries about 30 milligrams of nitriloside. Six or seven teaspoonsful will supply what our clinical investigators consider an adequate oral dose—one gram. It is best that the (beta)-glucosidase enzyme be completely heat inactivated in such material" (id. at 84). As discussed previously, this advocacy of the use of apricot kernels rather than a manufactured drug represents a change in the formulation of the product which is of particular importance because of the danger of toxicity associated with oral ingestion of apricot kernels.

The Commissioner concludes that drugs called variously Laetrile and amygdalin have no set composition, their makeup varies depending upon the manu-

facturer and the time of manufacture. It thus appears that any drug in use on October 9, 1962 was different in composition from Laetrile as used, or proposed to be used, today.

## *2. Investigational Use*

The record is clear that use of Laetrile (amygdalin) on October 9, 1962 was for investigational, not commercial, purposes. This fact is borne out by legal documents concerned with each of the two major figures in its development—Dr. Ernst T. Krebs, Sr., and his son, Ernst T. Krebs, Jr.—and by other information in the record. Much of the evidence relating to the 1962 grandfather issue, like that relating to the 1938 grandfather issue, is not of the type which would be considered reliable evidence in a court of law. In many cases the "evidence" consists of hearsay which is not substantiated by any documentation. The record does contain, however, a sworn affidavit of Ernst T. Krebs, Sr. In this affidavit (R 183, Att. 13 at ¶ 7) Dr. Krebs describes his shipment in interstate commerce of various versions of his cancer cure, including amygdalin which he stated to have been sold after 1949 under the name of Laetrile, "up through 1962." Dr. Krebs states, "The above shipments were for investigational use only."

Ernst T. Krebs, Jr., and the John Beard Memorial Foundation were convicted in 1962, upon pleas of guilty, of charges of introducing and delivering for introduction in interstate commerce a new drug with-

out an approved new drug application (R 183, Att. 16, App. 17). The drug involved there was another unproved remedy, called by Mr. Krebs "pangamic acid" or "Vitamin B-15." Sentence of imprisonment on those charges was suspended and the defendants placed on probation for 3 years on the condition that they not manufacture, sell, offer for sale, hold for sale, or deliver or give away any "new drug." Mr. Krebs, Jr., obtained a special order which allowed him to ship 400 vials of Laetrile to the McNaughton Foundation in Canada, "for investigational use" provided the Canadian Food and Drug Directorate acquiesced in that shipment. In a supplemental order of June 28, 1962, Ernst T. Krebs, Jr., was permitted, under certain detailed conditions, to deliver Laetrile to experts qualified by scientific training and experience to investigate the safety of drugs. The drug was not to be administered to any patient except one with extensive malignancy who was receiving Laetrile under Krebs' direction as of June 15, 1962. Thus, if Laetrile were in commercial use on October 9, 1962, and if the Laetrile involved were supplied by Mr. Krebs, Jr., he was in violation of this court order. Copies of the court papers involved in this criminal prosecution are found at appendix 17 to attachment 16 to R 183.

Use of a drug is investigational, as contrasted with commercial, when that use is for the purpose of determining whether, or demonstrating that, the drug in question is safe and effective. The record contains

no evidence to suggest that, contrary to the affidavit of Dr. Krebs, Sr., or to the court order binding Ernst T. Krebs, Jr., Laetrile (or amygdalin) was being used on October 9, 1962 for other than investigational uses.

"In 1953 the Cancer Commission of the California Medical Association investigated the claims made for the use of Laetrile in cancer treatment and condemned its use" (R 168, Att. "Vitamin Fraud"). The activities that led to the Medical Association action were apparently based upon Dr. Krebs' use of Laetrile. As shown by labeling collected during a 1952 FDA inspection, the Laetrile then in use was labeled, "Caution: New Drug limited by Federal Law to investigational use." (See R 184, Ex. 5.)

A submission to the record which contains much information about the use of Laetrile at about the crucial date of October 9, 1962 is the 1963 report of the California State Cancer Advisory Council entitled "Treatment of Cancer with Beta-cyanogenetic Glucosides ('Laetriles')" (R 183, Att. 16). While the Council concluded that use of Laetrile was not warranted in any context, its report does not contradict Krebs' claims that use was investigational at that time.

Other references to the use of Laetrile prior to 1962 do not specify whether or not the use mentioned was investigational, see R 183, Atts. 5, 6; R 307 at 1; R 64; R 174, Ex. 2; Tr. at 81-82.



A pamphlet entitled *Information for Physicians, Amygdalin The Non-Toxic Analgesic* provides information about what it states to be the experience of various doctors around the world in administering amygdalin to patients. Some of the statements indicate use by doctors before 1962—that use appears to be investigational and was not, with the exception of 10 cases reported by a New Jersey doctor, in the United States (R 183, Att. 10(b)).

The article by Levi et al., “Laetrile: A study of its Physiochemical and Biochemical Properties,” discussed above, refers to Laetrile as “a drug manufactured and distributed until recently for clinical trial in Canada and the United States to determine its value as a palliative in cancer therapy” (R 189, Att. at 1057).

In 1970 the McNaughton Foundation submitted an IND for Laetrile, which was disapproved by FDA (R 184 at ¶ 9). An IND is a notice, filed by persons interested in the development of a drug product, which seeks permission to distribute an unapproved new drug for the purpose of conducting clinical investigations of it in humans. Such clinical investigations must be completed to form the basis for an NDA for the drug. The fact that Laetrile’s proponents were still seeking to investigate its use in 1970 is additional evidence that any use of the drug on October 9, 1962 was investigational.

### 3. *Conditions of Use in Labeling*

In order to qualify for the 1962 grandfather clause, Laetrile (or amygdalin) would need to “be intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on” October 9, 1962 (section 107(c)(4) of Pub. L. 87-781). Conditions of use include, among other things, what the drug is recommended for, how it is to be administered, and in what quantities it is to be administered. Under the statute, any change in those conditions from October 9, 1962 to the present disqualifies the drug from exemption. (See *United States v. Allan Drug Corp. supra.*) Here, no submission contains either labeling now in use or proposed for use, or labeling used on October 9, 1962.

Since no labeling in use on October 9, 1962 has been submitted, the indications found in labeling in use in years prior to that time will be discussed as illustrative of the variation in proposed conditions of use apparent in the record. The Commissioner will then review labeling from dates after October 9, 1962. As the following discussion demonstrates, not only do the proposed conditions for use of Laetrile (amygdalin) vary from before October 9, 1962 to after that date, no two sets of labeling propose the same conditions.

#### Before October 9, 1962

A new drug application (NDA) submitted to FDA by the John Beard Memorial Foundation and Ernst T. Krebs, Jr., on October 3, 1962 indicates that Lae-

trile was a lyophilized water-soluble powder for use in the palliation of human cancer. Excerpts from the NDA, attached as Exhibit B to R 201, provide information concerning its intended uses: It was to be administered by injections of 1 gram each, which were to be either every day or every second day and either intravenously or intramuscularly. Intravenous administration was stated to be preferred. The average administration was stated to be every other day for a total of 10 injections. Apparently, a total of 20 grams of Laetrile were expected to be administered. Dosages; frequency, and route of administration are described as varying widely with each individual case. The application indicated that Laetrile often produces a temporary hypotensive reaction shortly after injection, especially in hypertensive patients. Laetrile is not indicated for use to the exclusion of surgery, radiation, or other chemotherapeutic substances where those find any indication.

The proposed labeling in the NDA is, of course, not an example of labeling in commercial use at the time of the NDA's submission. The NDA does, however, state the indications which Mr. Krebs, Jr., thought to be most appropriate for the use of Laetrile at that time. Thus, if Laetrile had been commercially used at that time, it is reasonable to believe that the indications proposed in the NDA would be the ones proposed in any labeling used for such a commercial product.

An article by Dr. Krebs, Sr., and Dr. Arthur T. Harris, entitled "The Treatment of Breast Cancer

With Laetrile By Iontophoresis" (copyright 1955 by the John Beard Memorial Foundation) (R. 183, Att. 7) proposes three different methods of utilizing Laetrile. At page 30, the three main methods of administering Laetrile and its auxiliary Beta-glucosidase are described as: (1) Parenteral administration (injection into the muscle), (2) iontophoresis, discussed below, and (3) tamponade.

Perhaps the most bizarre of the proposed methods of administration for Laetrile is "Iontophoresis". This new procedure developed by the senior Krebs for treatment of cancers "especially in the breast" is described as "infinitely more effective and thorough." The procedure is described as follows:

It is to force by galvanic current the Laetrile through the skin and into as well as between the individual cancer cells. The apparatus we use is a simple galvanic instrument (or, preferably, one of the modern instruments with resistors instead of tubes). The positive pole lead goes to the tumor site—the breast—the negative to the back. The solution of Laetrile is soaked in gauze and covered by a block tin electrode, then positioned firmly over the tumor. The negative pad, well moistened, is positioned on the back, and the current turned on. Slowly the amperage is raised to 10 milliamperes then 15, never more than 20 except in a very thick chest wall. In fifteen to thirty minutes, depending on the size of the growth, the pad has become almost dry; the Laetrile has been driven into—not around—the cancer cells (id. at 26-27).

The action of iontophoresis is described in more detail on pages 30-31. Apparently it is expected that the iontophoresis therapy will liquify the tumor mass, and a physician will thus be able to draw out, with an aspirating needle, the "cancer-juice" before administering the next iontophoresis treatment (id. at 32). Iontophoresis therapy involves administration every 2 to 5 days (id. at 31).

This article, which has been quoted and referred to previously, explains some of the history and theories of Laetrile's use. The article promotes the "Howard Beard Anthrone Test" for the diagnosis of cancer (id. at 34). This test involves analysis of the urine of the patients (see id. at 16-19). The authors recommend against biopsies to determine whether tumors are malignant (id. at 27-28). The authors state their opposition to surgery prior to "control" of the cancer by Laetrile (id. at 35).

Laetrile (amygdalin) is apparently currently in use as an oral medication. Nothing in the record, other than conclusory statements of the most general kind, indicates that any version of the drug was in use as an oral medication on October 9, 1962. The only statement that such a drug was ever used orally before that date which purports to be based on first-hand knowledge is the statement of Charles Gurchot, Ph.D. (R 302, Ex. L at ¶ 8), that between 1933 and 1934 a Dr. Lewis administered amygdalin orally as well as intramuscularly and intravenously. Dr. Gurchot states that use in California, in which he participated between 1934 and 1945, involved adminis-

tration intramuscularly and intravenously (id. at ¶ 14). As discussed above in the section on the 1938 grandfather clause, the "amygdalin" Dr. Gurchot states he was involved in using is different from that used at later dates.

After October 9, 1962

Variations in the conditions for use of Laetrile (or amygdalin) proposed in its labeling continued after the critical October 9, 1962 date. In 1965, an FDA inspection of Krebs' Laboratories produced labeling for Laetrile which suggested a new set of conditions for its use (see, generally, R. 201, Ex. C.). The labels on the packages of the drug stated "For raising hemoglobin index and red count[;] relieves pain due to malignancy." (Similar labels were obtained by California State health officials in 1971 (R 183, Att. 9).)

In a pamphlet published by Krebs' Laboratories, obtained in the 1965 inspection, injections at various sites were indicated for various types of cancer—brachial vein for cancer of lungs; brachial vein and innominate artery for breast cancer; external carotid or one of its branches for cancer of the neck, thyroid, face, and temple area; brachial vein for cancer of liver, gastro-intestinal tract and the spleen; the vault of the vagina, the abdominal aorta, or the internal iliac arteries for cancer of the uterus and ovaries; the scrotal sac for cancer of the prostate and testicle (R 201, Ex. C, II).



Two pamphlets obtained in the 1965 inspection are in fact inconsistent with each other in some instances, though the similarities in printing style indicate that they were printed at about the same time. One states the dose of Laetrile to be administered to be "(g)enerally speaking 10 mgs. per pound of patient's weight, with "occasionally" 15 mgs. per pound and "very rarely" 20 mgs. per pound (id.). The second states that: "The usual daily dose of Laetrile now is 20 mgs. of the glucoside Amygdalin for every pound of the patient's weight, or even twice this, particularly in bone cancer." Three gms. are recommended for a 150-pound person and 4 gms. for a 175-pound patient, i.e., over 20 mgs. per pound (id. at Ex. C, III). (While no labeling indicating such conditions was submitted, it should be noted that Dr. Binzel, at oral argument, talked of injections of from 9 to 15 grams of amygdalin at one time (Tr. at 363). The page proofs of Dr. Richardson's book indicate that he uses intravenous injections of "6-9 gms. or more" of Laetrile during the first month of treatment with intravenous or intramuscular injections of 3 grams thereafter (Tr. Ex. 1 at 124).)

More important, however, are the difference between the conditions recommended in the labeling collected in 1965 and those in that submitted with the 1962 NDA. In the 1962 NDA, Laetrile was to palliate, not to cure; in the 1965 labeling it is stated: "Laetrile does not palliate, it acts chemically to kill the cancer cells selectively without injury to the normal tissues of the body" (R 201, Ex. C). While the

1962 NDA stated that Laetrile was not indicated to the exclusion of other recognized cancer therapies, the labeling collected in 1965 states: "The less drugs and medicines given, during the Laetrile treatment the better. What should be especially avoided is sulphur and sulphur drugs and *other cancer therapies*, \* \* \*" (emphasis added) (id.). Even more frightening to those who are concerned that utilization of therapies of proven effectiveness will be delayed until too late because of use of Laetrile is the statement in the pamphlet in use in 1965 that: "Being harmless \* \* \* Laetrile should be used first instead of last as generally has been done when everything else has been tried and hope is gone" (id.). An affidavit submitted by Dr. Robert S. K. Young describes the medical importance of the numerous variations between the 1962 labeling and that of 1965 (see ¶ 11 of R 201).

The labeling discussed, which bears the name of Krebs Laboratories and of Dr. Krebs, Sr., appears as Ex. C to R 201. It should be noted that there is no copyright or other date on the labeling that was found in Dr. Krebs' establishment in 1965. One of the pamphlets, that which contains some of the statements quoted above, is described as a "pre-1963 pamphlet" in the affidavit of Dr. Sherwood Lawrence (R 183 at 4). It appears as attachment 8 to that affidavit.

A pamphlet published by the McNaughton Foundation suggests intravenous dosages of amygdalin of from 3 to 6 grams a day administered over a 24-hour period (R 183, Ex. 10b at 5). That pamphlet, which

cites references dated May 11, 1970 and thus must have been published thereafter, described the use of amygdalin as an analgesic, yet also indicates that the drug inhibits the growth of malignancies (id. at 1).

The record contains labeling for Laetrile (or amygdalin), which was in use after October 9, 1962, which clearly recommends oral administration of the drug. See R 183, Att. 10a—capsules, 400 mg.; R 183 Att. 4c—capsules, 400 and 500 mg.; R 183, Att. 10b—amygdalin tablets which may be broken up and added to drinking water or food ( $\frac{1}{2}$  to 2 grams per day recommended); R 183, Att. 10d—"Magydalin" capsules with 500 mgs. of "pure crystalline LAETRILE (amygdalin)".

While in 1962 Laetrile was proposed in the NDA as a palliative, the labeling in the record makes clear that it has been touted since that time as a treatment for cancer (see R 183, Att. 10a; see also R 201, Ex. C, discussed above). Mr. Krebs, Jr., claims Vitamin B-17, which may be or may contain Laetrile, to be "antineoplastic" and to be instrumental in "therapy" for cancer (Journal of Applied Nutrition, Vol. 22, "The Nitrilosides (Vitamin B-17)—Their Nature, Occurrence and Metabolic Significance (Antineoplastic Vitamin B-17)," at 75, 81 (R 183, Att. 10c).

In a transcript dated November 18, 1974, prepared by FDA, of a film entitled "World Without Cancer", produced by the proponents of the use of Laetrile, the claim is made that 15 percent of persons

with advanced metastasized cancer will be saved by "vitamin therapy," which from the context includes vitamin B-17 (Laetrile). The film claims that, of those with cancer diagnosed early, at least 80 percent will be saved by vitamin therapy. Of those who are healthy with no clinical evidence of cancer, the film's narrator states that close to 100 percent can expect to be free from cancer as long as they utilize vitamin B-17. The use of the term "vitamin B-17" indicates that the film was made after 1962, since Laetrile was not claimed to be a "vitamin" until after that time (see, generally, exhibit 2 to R 198).

As discussed above, to qualify for exemption from the "new drug" definition of 21 U.S.C. 321 (p) pursuant to the "1962 grandfather clause," the proponents of Laetrile (or amygdalin) would need to show among other things that the drug in question is now "intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on" October 9, 1962. No evidence in the record shows either that the drug was used or that any conditions of use were recommended for it on that date. Evidence in the record indicates that conditions of use recommended prior to the critical date not only conflict with each other, but also conflict with recommendations after that date which themselves conflict with each other. The Commissioner concludes, on the basis of the evidence in the record, that Laetrile as now known is not intended solely for use under conditions recommended in labeling on October 9, 1962.

#### 4. *Lack of General Recognition of Safety in 1962*

As discussed above, a drug could not escape new drug status under the "1962 grandfather clause" if it were a "new drug" on October 9, 1962. To have been exempted from new drug status on that date, Laetrile (or amygdalin) would have to have been "generally recognized among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof" (21 U.S.C. 321(p)(1) (1962)), and that general recognition would have to be based upon use other than investigational use (21 U.S.C. 321 (p) (2) (1962)). The Commissioner has elsewhere discussed the evidence that demonstrates that Laetrile and amygdalin (to the extent that they are different) are not now generally recognized by qualified experts as safe for use under the conditions prescribed, recommended or suggested in their labeling. While the present lack of general recognition of the substances would not necessarily demonstrate that they were not so generally recognized in 1962, that fact does provide evidence of the earlier lack of recognition.

The evidence in the record provides a number of independent grounds upon which the Commissioner concludes that Laetrile (or amygdalin) was not generally recognized by experts in drug safety evaluation as safe on October 9, 1962. That conclusion is supported (1) by the proven lack of a number of prerequisites to such general recognition: lack of knowl-

edge among such experts generally of Laetrile's use, of Laetrile's formulation, and of the proposed conditions of Laetrile's use; lack of data published in the scientific literature supporting Laetrile's safety as a cancer drug; and lack of scientific testing sufficient to show safety; (2) by statements in the record by experts in the evaluation of the drug safety that Laetrile was not generally recognized as safe as a cancer drug by themselves and their peers on October 9, 1962; and (3) by abundant evidence that Laetrile was not generally recognized by appropriately qualified experts to be effective in cancer therapy on October 9, 1962. The Commissioner concludes that the showing in the record on each of these points is itself sufficient to demonstrate that Laetrile (or amygdalin) was a new drug in 1962.

(a) *The Prerequisites.* (i) *Lack of General Knowledge of Use.*—A number of submissions to the administrative record indicated that the use, and the details of the use, of Laetrile or amygdalin were simply not generally known to the community of experts in the safety evaluation of drugs on October 9, 1962. Thus, there could not be any sort of "general" recognition of the substances' safety in 1962. (See, e.g., the oral testimony of Dr. Rhoads, the national chairman of the National Cancer Advisory Board (Tr. at 110-111; Tr. Ex. 5); oral testimony of Dr. Carr, professor in medicine at the Mayo Medical School (Tr. at 181).)

(ii) *Lack of General Knowledge of formulation.*—The variability in, and uncertainty about, the com-



position of the drug in use at that date (discussed in detail above) means that "general recognition" of the drug's safety by experts in drug safety evaluation would be impossible. The fact was recognized in *Durovic v. Richardson*, *supra*, 479 F. 2d at 251, in which another unproven cancer remedy was ruled not to be exempted from regulation by the 1962 grandfather clause.

(iii) *Lack of General Knowledge of Conditions of Use Suggested*.—Equally important, the variation in and uncertainty about the conditions of use suggested in the labeling of Laetrile (or amygdalin) on October 9, 1962, also discussed in detail above, means that such general recognition could not have existed. The law as of that date is clear that general recognition must be of safety "for use under the conditions prescribed, recommended, or suggested in the labeling" of the drug (21 U.S.C. 321(p)(1) (1962)). If experts throughout the country could not have known of those conditions of use, recognition of safety by them could not have existed.

(iv) *Lack of Safety Data in Scientific Literature*.—The existence of published data available in the scientific literature on the safety of a drug is a prerequisite to general recognition by experts of that drug's safety within the meaning of 21 U.S.C. 321 (p). *Weinberger v. Bentex Pharmaceuticals, Inc.*, *supra*, 412 U.S. at 652; see *United States v. 41 Cases, More or Less*, 420 F. 2d 1126, 1130 (5th Cir. 1970); *United States v. 1,048,000 Capsules, More or Less*, *supra*, 347 F. Supp. at 771. The record lacks any

reference to any such published data available to experts on October 9, 1962.

In fact, the record demonstrates that, while data showing the lack of Laetrile's effectiveness have been published in the scientific literature, data upon which an expert in the evaluation of drug safety could make a judgment that Laetrile was safe for use in cancer therapy do not exist in the scientific literature available to experts generally even today.

(v) *Lack of Showing of Safety by Adequate Testing*.—As noted in the sections of this opinion dealing with the new drug issue, the Supreme Court has held in *Weinberger v. Bentex Pharmaceuticals, Inc.*, *supra* that "general recognition," as those terms are used in 21 U.S.C. 321(p), requires the same type of showing of safety and efficacy necessary for approval of an NDA pursuant to 21 U.S.C. 355(d). For approval of an NDA prior to October 9, 1962, the application was required to contain "adequate tests by all methods reasonably applicable to show whether or not such drug is safe" for its intended uses, and those tests were required to in fact show that the drug was safe (21 U.S. 355(d) (1962)). It appears from the record that no such tests existed for Laetrile (or amygdalin) on October 9, 1962. Were there a question about the lack of such studies, that question could be resolved by the fact that, at approximately the time in question, NDA's for Laetrile and for a combination of Laetrile and iodine were submitted to the FDA. Both applications were declared to be incomplete because of the lack of required data to show

safety and effectiveness. (See, generally, the letter from John L. Harvey, FDA Deputy Commissioner, to K. F. Ernst, M.D., April 30, 1963 (R 183, Att. 16, App. 18).)

(b) *Statements by Experts.* Even setting aside the above important prerequisites to general recognition, the evidence in the record that Laetrile was not generally recognized as safe by experts in the evaluation of drug safety on October 9, 1962 is extremely strong.

The plethora of statements of experts in drug evaluation that Laetrile (or amygdalin) is not now generally recognized as safe is discussed elsewhere. Some of the experts focused upon the October 9, 1962 date. (See affidavit of Dr. Emil J. Freireich: "Neither amygdalin nor any other cyanogenic glycoside was generally recognized as safe for any (use in the treatment of cancer or prophylaxis against cancer or relief of pain associated with cancer, or for any medical use) on October 10, 1962" (R 390 at ¶ 10; accord affidavit of Dr. Daniel T. Carr, (R 176 at ¶ 15.) For a similar statement that Laetrile was not generally recognized as safe by appropriately qualified experts in 1962, see affidavit of Dr. Carl M. Leventhal (R 184 at ¶ 13).

Even more compelling evidence on this question can be gleaned from statements of experts in drug safety evaluation made near the October 9, 1962 date. Fortunately, at just about that date the State of California Cancer Advisory Counsel was polling

just that type of expert concerning Laetrile (R 183, Att. 16 at 37-38). (Since the Krebs Laboratory was located in California, it would seem that experts in the California area would be most likely to be aware of recognition of Laetrile or amygdalin's safe use as cancer therapy.) The experts polled, representing each of the medical schools in the California university system, were asked about the drug's efficacy rather than their views on the question of the safety of Laetrile's use in cancer therapy. Clayton G. Loosli, M.D., Dean of the University of Southern California School of Medicine, speaking for the members of the school's faculty, indicated that Laetrile, while extensively investigated, was in the unanimous opinion of the faculty without value in the treatment of human cancer. He stated that "further, we consider its use not only not valuable even as a placebo but harmful in that use of Laetrile prevents patients from receiving what otherwise might be an effective modality of treatment" (id., App. 10). J. B. deC. M. Saunders, M.D., Dean of the University of California School of Medicine at San Francisco, speaking for the clinical staff of his medical school, gave their opinion that the use of Laetrile was of no value in the treatment of cancer. He said "(i)t may not only delay or interfere with conventional therapy (surgery and radiation) but indeed could seriously jeopardize whatever chances the patient may have for cure. The unscrupulous use of unproven cancer 'remedies' such as Laetrile tragically increases the

human suffering already associated with cancer (id.).

The only evidence submitted by proponents of Laetrile that experts qualified to evaluate the safety of drugs generally recognized the drug as safe when used in cancer therapy were two affidavits by Charles Gurchot, Ph.D., and Chauncey D. Leake, Ph.D., (R 302, Exs. K and L). The Gurchot affidavit states in paragraph 14 that amygdalin in liquid and solid form was used prior to 1962 (between 1934 and 1945) by Gurchot, under the supervision of five named medical doctors at the University of California Medical School at San Francisco (R 302, Ex. L). This amygdalin was, according to his statement, administered "on patients intramuscularly and intravenously" (id.). At the same time, the amygdalin preparation he used, he states, was used by "about a dozen physicians throughout California through the University of California Medical Schools and as recommended by members of the Hospital Staff of the University of California Medical School at San Francisco" (id.). Gurchot states that these physicians were qualified by medical and scientific training and professional experience to evaluate the safety of substances such as amygdalin and that they recognized it as safe (id.). The Gurchot affidavit should be compared, in the first instance, to the 1962 statement, already discussed, of the Dean of the University of California Medical School at San Francisco, which states, "Laetrile is not, *nor has it been*, in clinical use or in experimental trials in this institu-

tion \* \* \*" (emphasis added) (R 183, Att. 16, App. 10 at 8).

Even were the Commissioner to credit Dr. Gurchot's statement, he would have to conclude that, whatever had happened in the years 1934-1945, that experience did not form a basis for general recognition by qualified experts of safety in 1962, since even the faculty of the medical school in which Gurchot claimed the experiments had taken place had no knowledge of them. It should also be noted that, as discussed in the section on the 1938 grandfather clause, the "amygdalin" Gurchot could have been using would not have been the same substance in use today. His evidence, in addition, speaks only of investigational, as opposed to commercial, use of the drug—an improper basis for "general recognition" (see discussion above). In light of these facts, and of the other information in the record on this issue, Gurchot's statement in paragraph 16 of his affidavit indicating his belief that the general recognition of safety requirement for exemption from new drug status did exist for amygdalin on or prior to October 10, 1962 must be questioned.

The affidavit of Chauncey D. Leake, Ph.D., indicates that he is familiar with Dr. Gurchot's use of amygdalin in the mid-1930's and 1940's at the University of California Medical School Hospital in San Francisco. He states that at that time, i.e., in the 1930's, "it was generally held by physicians and other scientists familiar with it, that amygdalin was safe when used in the treatment of cancer as well



as in its use as an expectorant or cough suppressant" (R 302, Ex. K at ¶ 6). This conclusion does not, however, indicate recognition by anybody in 1962; it does not, as demonstrated elsewhere, deal with the drug presently being used (see affidavit of Dr. Krebs, Sr., (R 183, Att. 13)); it refers only to physicians and scientists "familiar with it", thus not addressing the question of whether recognition was general.

(c) *Lack of General Recognition of Effectiveness in 1962.*—Experts in the evaluation of the safety of a drug do not conclude that a drug is safe, if that drug is intended for the treatment of a life-threatening disease, if it has not been shown to be effective. The record illustrates a broad consensus of cancer researchers and physicians that Laetrile presents a grave danger to patients who might be helped by orthodox therapy. The concern is that such patients may be induced to turn instead to this ineffective drug, their disease may progress while effective therapies are forsaken, and the use of the ineffective cancer drug will inevitably and inexorably lead to the patient's death. (See, e.g., R 396 at 1; R 384; R 170 at ¶ 11; R 183 at 18; R 266, Ex. 3 at 865; R 192 at ¶ 14; R 193 at 1; and R 195 at ¶ 13.) Thus, even if it were shown, as it has not been, that experts in 1962 generally were aware of the drug, its formulation, its conditions of use, and of toxicity data concerning it published in the scientific literature, the alleged nontoxicity of Laetrile (or amygdalin) would not form a sufficient basis for general recognition of safety in 1962.

At the time of the 1962 amendments to the act, it was made clear, where drugs utilized for life-threatening diseases are involved, evidence of effectiveness is essential to proof of safety. The Senate report on the amendments stated:

The Food and Drug Administration now requires, in determining whether a "new drug" is safe, a showing as to the drug's effectiveness where the drug is offered for use in the treatment of a life-threatening disease, or where it appears that the "new drug" will occasionally produce serious toxic or even lethal effects so that only its usefulness would justify the risks involved in its use.

(S. Rep. No. 1744, 87 Cong. 2d. Sess., 1962 U.S. Code Cong. Ad. News 2884, 2891.) The report made it clear that the amendments were "in no way intended to affect any *existing authority of the (FDA) to consider and evaluate the effectiveness of a new drug in the context of passing upon its safety*" (emphasis added) (id. at 2892).

As the Court held, when dealing with a similar unproven cancer remedy, in *Durovic v. Richardson*, *supra*, lack of general recognition of the effectiveness of a drug intended for treatment of a life-threatening disease on October 9, 1962 means that general recognition of its safety could not have existed:

(A) drug offered for use in the treatment of cancer is now, and was before the amendments, a new drug unless it has achieved general recognition among the experts as safe and effective for such use (479 F. 2d at 250).

The evidence in the record overwhelmingly demonstrates that, among experts in the evaluation of the safety and effectiveness of drugs, Laetrile (or amygdalin) is not recognized as effective (see discussion above). It is a fair inference, absent any indication to the contrary, that a drug not recognized as effective now was not so recognized on October 9, 1962.

Again, however, the record supplies evidence of opinions of such experts given at almost exactly the time in question. As noted above, the medical schools in California were asked their opinions of Laetrile's effectiveness. Each of the medical schools contacted stated that Laetrile was never used in their institutions and that they concluded that it was not effective and had not been shown by testing to be effective. (See, in addition to the letters discussed above, letters from Dean David B. Hinshaw, M.D., Dean of Loma Linda University Medical School, Dr. M. H. Simmers, Coordinator, Cancer Training, California College of Medicine, Sherman M. Mellinkoff, Dean, University of California, Los Angeles Medical School.) These letters are printed as appendix 10 to R 183, Att. 16; see also R 183, Att. 16 at 38. The report states that Robert H. Alway, M.D., Dean of Stanford University School of Medicine, also indicated that Laetrile was of no value in cancer treatment and was not part of the treatment program at his medical school (R 183, Att. 16 at 38). The report also states that two other professors involved with cancer therapy and research concurred in this

evaluation (id.). The report of the California Cancer Advisory Counsel itself constitutes convincing evidence that at about the time of the crucial date, October 9, 1962, experts did not generally recognize Laetrile as safe for the treatment of cancer, in particular because it was considered to be a worthless treatment for a life-threatening disease. As has been pointed out elsewhere, no adequate and well-controlled clinical investigations, the prerequisite for general recognition by experts of a drug's effectiveness (*Weinberger v. Hynson, Wescott and Dunning, Inc., supra*) exists as to Laetrile. Thus, even were the testimony in the record on this question less conclusive than it is, it would be necessary to find that there was no general recognition by experts that Laetrile was safe for use for any purpose on October 9, 1962.

The Commissioner thus concludes that Laetrile (or amygdalin) does not qualify for exemption from the new drug provision of the act by virtue of compliance with the 1962 grandfather clause.

#### IV. THE POPULARITY OF LAETRILE

##### A. LAETRILE AND OTHER UNPROVEN REMEDIES

Laetrile, as far as is known, has nothing in common scientifically with any of the other "unproven" cancer remedies of the past.\* Yet the method of

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\* Dr. Ernst Krebs, Sr., though he thought people should be allowed to use his Laetrile, and a number of other remedies since forgotten by the public, is on record as stating that he could see no rationale for Krebiozen, the last of the highly publicized "unproven" cancer remedies (R 183, Att. 14 at 2).

promotion of the drug and the arguments advanced for its use are markedly similar to those of past cancer frauds.

### 1. *The History of Cancer Quackery in the United States*

Through the ages there have been literally thousands of supposed remedies for cancer, generally so outlandish that it seems incredible that people once believed in them. One historian of health quackery pointed out that the promotion of "unproven" cancer cures has a long history in this country:

Cancer quackery appeared in America during colonial times, one example being the alleged "Chinese Stones" vended by a purported Frenchman, Francis Torres, who hawked his cures from town to town. During the nineteenth century, an alert physician, Caleb Tichnor, bemoaned the breed of cancer quack, (each of whom offers) his "secret specific" to the panicked citizenry who, "like a drowning person grasping at straws seize upon the frail hope that is offered by the hand of ignorant charlatanry!" "Dr. Johnson's Mild Combination Treatment for Cancer" offered the first serious legal challenge to the 1906 Pure Food and Drug Act, requiring the Congress to enact the Sherley Amendment of 1912. At this same time, Dr. Arthur J. Cramp of the American Medical Association devoted fifty pages in his first *Nostrums and Quackery* volume to a detailed account of ten major cancer 'cures' deceiving the American people. Compiling a third volume in 1936, Dr. Cramp pointed to twenty-nine pur-

ported cancer cures, stating that "hardly a week has passed when the Bureau of Investigation of the American Medical Association has not received one or more letters in which the writers stated that they had discovered, or had in their possession, a 'sure cure' for cancer."

Nor has cancer quackery diminished as the twentieth century has progressed. Indeed, with the decline of contagious diseases, due mainly to the chemotherapeutic revolution, and the consequent rise of cancer into second place as a cause of death, cancer quackery has expanded. The 1971 edition of *Unproven Methods of Cancer Management*, published by the American Cancer Society, described fifty-four promotions offering hope to cancer sufferers but deemed devoid of value by ACS. The 1976 edition of *Unproven Methods of Cancer Management* cites in its appendix seventy-one such methods (R 400 at 1-2; see also R 400, Ex. 2).

Evaluation of approximately 60 of these methods may be found as attachments to R 400, Ex. 2.

Each decade seems to have an unproven cancer remedy that is promoted so effectively that it attracts a large following and becomes a cause celebre. In the 1940's and early 1950's, the Koch Antitoxins were heavily promoted as a specific cure for cancer. The Koch Antitoxins thesis, promoted by William F. Koch, M.D., advanced "the theory that cancer is caused by a microorganism resembling the spirochete of syphilis, which could be destroyed by a differential poison of his invention" (R 183, Att. 3 at 43). "The Koch medications, known collectively as Koch's Syn-



thetic Antitoxins or oxidation catalysts, were individually packaged in 2 ml ampules. Malonide and glyoxylide (were) claimed to be present in a concentration of one part in a trillion parts of water, and parabenzoquinone one part in a million parts of water" (id.). "Glyoxylic acid, of which glyoxylide is the anhydride (the resulting element after water is removed), is a normal constituent of the human body. About two grams are formed daily—at any given time there are about five milligrams in the human body, whether healthy or diseased. It would take a trillion 2 ml ampules of Koch's glyoxylide to equal the amount produced daily by the body, and two and one half billion ampules to equal the amount present in the body at any one time" (id. at 44). Even so, cancer patients paid as much as \$300 per injection for this worthless remedy (R 400, Ex. 2, ACS "Koch Antitoxins").

Another unproven cancer remedy whose promotion reached substantial proportions in the 1950's was the medications of Harry Hoxsey. Two liquid mixtures played the central role in the Hoxsey remedy. The "brownish black liquid" contained potassium iodide and "some of all of the following inorganic substances as the individual case may demand: Licorice, red clover, burdock root, stillingia root, berberis root, poke rot, cascara, Aromatic USP 14, prickly ash bark, (and) buckthorn bark (R 400, Ex. 2, ACS "Hoxsey Method"). The "pink liquid" was composed of lactate of pepsin and other ingredients (R 416, Ex. 6 at 368).

Hoxsey and his spokesmen were frank to confess that they did not completely know why his colored mixtures cured cancer. They asserted that they had been kept too busy treating cancer patients and fighting court battles to keep their clinic open "to spare the time, personnel, and facilities for objective study" (id. at 369). Hoxsey's hypothesis "held that a major chemical imbalance in the body caused normal cells to mutate into a cancerous form, and his medicines restored the original chemical environment, checking and killing the cancerous cells" (id. at 369). The proponents of the Hoxsey remedy, like the Laetrile proponents of today, condemned the only treatments then recognized as having value in cancer therapy. The Hoxsey proponents held that "X-ray and radium (had) no place in the treatment of cancer \* \* \*. They further upset basic cell metabolism rather than do anything to correct it" (id. at 369).

Harry Hoxsey promoted his unproven cancer remedy for more than 30 years until 1960, when after years of numerous local, State, and federal court actions, the sale of the Hoxsey medicines was stopped in the United States. At the time of the 1960 permanent injunction banning the sale of Hoxsey remedy at the Taylor Clinic, more than 10,000 patients were receiving the remedy. (See, generally, R. 400, Ex. 2, ACS "Hoxsey Method"; R 416, Ex. 6.)

In 1964 a California State government report stated that, at that time, "Possibly no other unproven treatment for cancer has recived so much public at-

tention or approbation as Krebiozen. This agent has been the subject of intense scrutiny by scientists and government officials, and loudly discussed by the press and by the general public. The events surrounding the introduction of Krebiozen as a potential cancer cure and the subsequent trials to test its capabilities produced an air of notoriety seldom seen in the medical world" (R 183, Att. 3 at 59).

Unlike Harry Hoxsey's backwoods herb remedy, Krebiozen, the most heavily promoted unproven cancer remedy of the 1960's, had an aura of high scientific prestige. The drug's principal proponent in the United States was Dr. Andrew C. Ivy, then Vice-President in charge of the Chicago Professional Colleges. Distinguished Professor of Physiology and Head of the Department of Clinical Science, University of Illinois (id.) Krebiozen was reportedly produced originally in Argentina by Steven Durovic, M.D., a Yugoslavian physician, and brought to the United States in 1949 (R 400, Ex. 2, ACS "Krebiozen and Carcalon"). "According to Dr. Durovic, the original 2 grams of powder, from which he said 200,000 doses were prepared, was obtained as an extract of the blood of 2,000 Argentinian horses which had previously been injected with a sterile extract of *Actinomyces bovis*, a microorganism which causes a disease called 'lumpy jaw' in cattle" (id.). "Food and Drug Administration analyses of Krebiozen ampules (showed) that those sold before 1960 (were) different from those sold in 1963, and that neither contain(ed) any of the powder identified in July

1963 by Dr. Stevan Durovic as Krebiozen, and found to be creatine monohydrate, which will not dissolve in mineral oil. \* \* \* analyses of Krebiozen ampules shipped before 1960 showed they contained nothing but mineral oil, while ampules shipped since then contained mineral oil plus minute amounts of amyl alcohol and 1-methylhydantoin, a derivative of creatine which will dissolve in mineral oil" (id.).

In 1963, a committee of 24 cancer experts was appointed by the Director of the National Cancer Institute to review clinical records on 504 patients treated with Krebiozen, and to recommend whether the Institute should sponsor clinical trials of Krebiozen. The committee unanimously concluded that Krebiozen was an ineffective cancer drug and strongly urged that no clinical trial be undertaken (id.).

In November 1964, Drs. Ivy and Durovic and other proponents of Krebiozen were indicted on 49 counts of violations of the Federal Food, Drug, and Cosmetic Act, mail fraud, mislabeling, making false statements to the government, and conspiracy. All of the defendants were acquitted in January 1966, after a 9-month jury trial (id.). Although the acquittal meant that the government did not prove its case beyond a reasonable doubt, it did not have any bearing on the question of whether Krebiozen was a safe and effective cancer drug. As an unapproved new drug, its distribution in interstate commerce remained illegal. In spite of the acquittal, the Krebiozen boom collapsed shortly thereafter.

2. *Similarities Between Laetrile Promotion and That of Other Recent "Unproven" Cancer Remedies*

The promotion of Laetrile in the 1970's is completely in character with the historical pattern of the promotion of other unproven cancer remedies such as the Koch Antitoxins, the Hoxsey method, and Krebiozen. These characteristics include the following:

(1) The proponents "don the mantle of science while at the same time traducing the reputations of scientists of their day" (R 400 at 3).

(2) The proponents claim that "prejudice of organized medicine hinders their efforts" and they "challenge established theories and attack prominent scientists with bitter criticism" (R 400, Ex. 2 "Unproven Methods of Cancer Management—1976" at 3) (hereinafter cited as "Unproven Methods").

(3) The proponents "cite examples of physicians and scientists of the past who were forced to fight the rigid dogma of their day" (id).

(4) The proponents rely mainly on testimonials and anecdotes as evidence that their remedy is a safe and effective cancer therapeutic agent (see R 400 at 4).

(5) The proponents "do not use regular channels of communication (current, reputable scientific journals) for reporting scientific information" (R 400, Ex. 2 "Unproven Methods" at 2-3). The main channels of communication are the mass media, popular journalism, and word of mouth (see R 400 at 4-5).

(6) The proponents' "chief supporters tend to be prominent statesmen, actors, writers, lawyers, even members of state or national legislatures—persons not trained or experienced in the natural history of cancer, the care of patients with cancer, or in scientific methodology," (see R 400, Ex. 2 "Unproven Methods" at 3.)

(7) The proponents often offer a simplistic theory for causation of the disease frequently involving claims that dietary management can counteract virulent pathologic processes (R 266, Ex. 3 at 865).

(8) The proponents' remedy is "easy and pleasant, compared with the frightening therapies wielded by orthodoxy, the surgical knife, harsh chemical drugs, poisonous radiation" (R 400 at 8).

(9) The proponents claim that the mode of administration of the drug and the method of treatment can only be learned from them (R 400, Ex. 2, "Proven Methods" at 3).

The record illustrates the remarkable conformity of the Laetrile promotion to this pattern:

(a) *Mantle of Science*.—Throughout history, promoters of unproven cancer remedies have couched the explanation for the remedies in pseudoscientific terms. "Impressive and plausible to the layman, such arcane explanations, to true scientific specialists, came off as nonsensical balderdash" (R 400 at 3). The promoters of Laetrile have presented a series of shifting theories to explain the alleged anticancer activity of Laetrile. These theories have been examined in detail above. (See, generally, R 218.)



(b) *Attacks on the "Establishment."*—The proponents of Laetrile have often accused government agencies and organized medicine of making untruthful and irresponsible statements regarding the experimental evidence of Laetrile's anticancer activity. (See, e.g., R 302, Ex. A at 14-16; R 509 at 3-4.) In other instances, proponents of Laetrile have chastized the orthodox methods of cancer treatment and management, i.e., surgery, radiation, and chemotherapy. (See, e.g., Tr. at 16-27, 297-316, and 417-426.)

The most vocal arguments challenging established orthodox treatments have been concerned with the issue of freedom of choice, discussed elsewhere in this opinion. These arguments, many of them from cancer patients or their relatives and friends, hold that the "bureaucracy" has no right to interfere with the physician-patient relationship by withholding from them a treatment in which they believe and which they want. (See, generally, Tr. at 55-56, 255-256, and 454-456.)

(c) *Claimed Parallel with Scientific Pioneers.*—To combat criticism from the established medical societies and government agencies that Laetrile had not been shown to be safe and effective, its proponents compare the originators of the drug and physicians who prescribe Laetrile with earlier scientists who were persecuted and ostracized for their scientific theories: Copernicus, Newton, Freud, Galileo, and Semmelweiss. (See, e.g., R 318 at 61-63; R 198, Ex. 2 at 3-5).

(d) *Reliance on Testimonials.*—As previously discussed, the proponents of Laetrile rely on testimonials

and anecdotes as evidence that the drug is safe and effective in the treatment of cancer. In reviewing the administrative record, the Commissioner has not encountered even one study that meets the legal and scientific standards for making a determination that Laetrile is safe and effective. Proponents claim that physicians using Laetrile are too busy treating patients to be able to maintain records needed to document adequately the case histories they present. (See, e.g., Tr. Ex. 1 at 117.)

(e) *Lack of Scientific Publication.*—Good science demands that evidence that a drug is safe and effective be presented in a manner whereby that evidence can be reviewed and evaluated by other scientists. Usually this evidence is published in scientific journals and presented for discussion at symposia and other meetings. Historically, "the main reliance of unorthodox promoters rests on the anecdotal evidence of testimonials from laymen, and the main channel for reaching an audience is through the mass media. In earlier days newspaper advertising trumpeted the promise of cancer cures, bolstered by the faces and words of grateful testifiers, not infrequently already dead of the disease" (R 400 at 4-5). The proponents of Laetrile have relied heavily on popular journalism, advertisements, radio and television, "health" organizations and word of mouth to spread their claims that Laetrile is a safe and effective anticancer drug. (See, e.g., R 318; R 302, Ex. A and H; R 198, Ex. 2.) A number of experts active in the management of

cancer have submitted testimony stating that the scientific literature contains no reports of adequate, well-controlled studies upon which Laetrile can be regarded as generally recognized as safe and effective. (See, e.g., R 185 at 5; R 186 at 4; R 390 at 6.)

(f) *Nonexpert Supports.*—The proponents of Laetrile are well-organized and, through organizations such as the Committee for Freedom of Choice in Cancer Therapy, have conducted active campaigns to move the discussion of the safety and effectiveness of the drug from the scientific to the political arena. These organized efforts have encouraged cancer patients and others to write their local, state, and congressional representatives demanding that Laetrile be “legalized.” These efforts are addressed not to discussions of the scientific merits of Laetrile as a cancer drug, but rather to the issue of “freedom of choice” discussed elsewhere in this opinion. Such action on the part of the Laetrile proponents is typical of other unproven cancer remedies. Failing to win acceptance in the established medical community, proponents seek sympathetic allies in places of political power. (See R 400 at 6-7.)

(g) *Simplistic Theories of Causation and Reliance on Diet.*—The latest claims being made for Laetrile are that it is a “vitamin,” and that cancer is a vitamin deficiency disease. The basis for these claims is discussed elsewhere in this opinion. It is sufficient to note here only that this simplistic theory of cancer prevention and treatment is common to other unproven cancer remedies. Cancer patients are told

that they can cure or control their cancer by strict adherence to a special diet that includes a special vitamin” even though this “vitamin” is not recognized by nutritional experts. (See R 266, Ex. 3 at 865-66.)

(h) *A Painless Cure.*—Laetrile, like other unproven cancer remedies, is promoted as a harmless cancer remedy free of the side effects associated with orthodox methods of treatment such as radiation and chemotherapy. Many of the statements submitted by cancer patients and their relatives and friends reflect the proponents’ claims that Laetrile is free of side effects. (See, e.g., R 17; R 48; R 137.)

(i) *Only Proponents Can Effectively Use the Drug.*—In common with the supporters of other unproven cancer remedies, the proponents of Laetrile stress, as did Robert W. Bradford of the Committee for Freedom of Choice in Cancer Therapy, that “you” do not and cannot expect to get results from Laetrile treatment unless you are a trained metabolic physician” (Tr. at 349). These arguments are used to explain why orthodox physicians (i.e., those not trained in the proper use of Laetrile) do not see any evidence of Laetrile’s effectiveness as a cancer drug.

#### B. WHY DO PEOPLE USE LAETRILE?

Throughout history persons afflicted with cancer have turned away from the medical establishment to a series of what most euphemistically might be called “unproven remedies.” Laetrile is the most recently publicized of these remedies, but, as the discussion

above illustrates, it follows on the heels of other widely publicized therapies such as Krebiozen and the Hoxsey cure. Thoughtful persons have questioned the reasons for this troubling phenomenon. Why do people bet their lives, or the lives of their loved ones, on a therapy which is rejected by almost everyone trained and experienced in cancer research and treatment?

Much evidence in the record addresses this question. The answer lies in the fear that cancer engenders—and that proven therapies for cancer engender—and the need of patients and families for hope in a situation where the hope offered by the legitimate therapies is often modest. The use of “unproven remedies” is, in the opinion of observers, in large part attributable to the loved ones of the cancer victim, in whom both fear and the need for hope are magnified by sympathy and by the guilt that one feels at being unable to relieve the suffering of a person one loves. This situation is, unfortunately, skillfully exploited by the purveyors of “unproven” cancer remedies, of which Laetrile is only the most publicized.

#### *1. The Emotional Reaction to Discovery of Cancer*

“[W]hen cancer afflicts an individual, he is frequently faced with a circumstance which is virtually without hope. First of all, the cancer patient must be terrified by the diagnosis \* \* \*. It would be enough to terrify any lay person to simply be told that he has

cancer. But more important than that is the fact that once he is told that he has cancer, he is told by the doctor that the treatments that we have available are very often disfiguring; they can be painful; they can be unpleasant; they can even be risky” (Tr. at 204).

The cancer patient must thus cope with two wounds simultaneously. The first is to the body itself (R 423 at 1). “The other wound is to the psyche, reflected in the loss of the feeling of being invulnerable, a feeling which is basic to ordinary day by day living” (id.). The cancer patient senses suddenly that the future is limited. Social and work mobility are seen as curtailed; so are the patient’s functional role in the family and the community. In addition, the patient senses a new dependence on others and may fear that he or she will become a burden on the family (id. at 2). “The initial psychological status of the patient and family is characterized by disorientation, anxiety, guilt, fear of pain and suffering” (R 421 at 1).

Dr. Robert C. Eyerly, Chairman of the American Cancer Society’s Committee on Unproven Methods of Cancer Management, states that, “Indeed, we’ve found that the major reason cancer patients use Laetrile is fear \* \* \* fear that the disease is incurable, that surgery or other therapy is mutilating, and that the medical profession is not to be trusted” (R 173, Att. “Laetrile: Focus on the Facts”).

In this climate of anxiety and fear, the medical establishment—which, unlike the proponents of “unproven” remedies, feels an obligation to be honest



with the patient and his family—cannot always offer hope: “[P]robably the most important factor (explaining why cancer patients choose to use Laetrile) has been the failure of modern medicine and technological advances to cure or adequately control some cancers. These unfulfilled expectations lead patients to disappointments in standard medicine and to attempt a cure of their disease by pseudoscientific methods” (R 398 at ¶ 9).

Physicians, trained in the saving of life and the alleviation of suffering but unable, in some cases, to do either with cancer patients, may contribute to the frustration. “Many patients sense a feeling of frustration and hopelessness conveyed, perhaps unconsciously, by the physician who tells them the nature and probable outcome of their disease—a natural feeling on the part of the physician who is discouraged by his recognition that he cannot cure the patient. Patients sensing this hopelessness frequently are unwilling to ‘abandon hope’ and therefore seek (unorthodox therapies)” (R 190, Ex. 4, Editorial at 327). Glen W. Davidson, Ph.D., Chairman of the Department of Medical Humanities, Southern Illinois University School of Medicine, testified that, “\* \* \* when primary emphasis for treatment is placed on ‘cure’ and the physician’s abilities, rather than on ‘coping’ and the patient’s abilities, the patient is placed in an inappropriate and ineffective dependency relationship. When the physician can no longer promise ‘cure’ and then attempts to refer the patient out

of his practice, or leaves the patient to institutional care of others, the patient feels abandoned. The patient has already had his coping abilities undermined. And many patients react to unfulfilled expectations and violated trust with anger and panic” (R 387 at 2).

A patient facing cancer and the lack of positive assurance from the physician that the cancer can be cured may simply give up hope that what the physician can do for the patient can work. This lack of confidence in proven remedies is tragic in an era when, in the case of many cancers, a significant percentage of patients can be cured or have their lives extended. See, e.g., R 173, Att. ACS, 1977 Cancer Facts at 3. Laetrile’s proponents expend great efforts to encourage this feeling. Much of the oral argument of Laetrile proponents in this proceeding was addressed not to the effectiveness of Laetrile but to the ineffectiveness of proven remedies (see, e.g., Tr. at 16 et seq.; Tr. at 228). With real hope extinguished, the use of Laetrile or other unproven remedies is a way of avoiding an acceptance on a conscious level of the consequences of the disease: “The decision to use Laetrile indicates that, at the subconscious level, patients and their families have given up on conventional therapy and, in fact, have accepted the inevitability of death. On the more superficial level, patients choosing Laetrile are persons who believe that they do not require the use of sophisticated, anti-cancer treatments. This reflects an ambivalence which many patients feel at the time they are required to make

decisions about cancer therapy. If patients can maintain denial about the seriousness of their cancer, then they can permit themselves to experiment with a bizarre apricot-extract, such as Laetrile" (R 433 at ¶ 13). "Human beings have become accustomed to using the psychological techniques of denial in dealing with real problems" (R 390, Ex. 3 at 386). "The decision to use Laetrile is, in essence, an attempt 'magically' to avoid the reality of cancer" (R 433 at ¶ 9).

## 2. *The Role of Loved Ones*

Patients with a diagnosed malignancy frequently encounter ostracism in their private, social, and vocational roles (R 387 at 1). At this point, the caring of loved ones and their sympathetic willingness to continue to associate with and to share the suffering of the cancer patient assume great importance to the patient. This caring relationship, quite understandably, leads to a dependence by the patient on the loved one and a corresponding feeling of responsibility in the nonpatient: "Many patients in their initial response to cancer diagnosis surrender control to those closest to them, further complicating the issue of informed choice. Highly anxious relatives with little or no medical understanding of cancer as a disease entity fall prey to the emotional appeal of the proponents of Laetrile" (R 421 at 2). "Cancer patients are most vulnerable to the manipulations of others when they feel they are (1) being abandoned,

(2) unable to control pain, and (3) unable to maintain a 'sense of dignity' by being able to make decisions for themselves. Attempts at guarding oneself from all three fears are often incompatible. Many cancer patients feel they are in a 'double-bind.' If they don't follow their physician's treatment plan, the disease process won't be arrested. If they don't follow the competing, and often contradictory advice from relatives and friends, they will be abandoned. And if they assert their own feelings they will be ostracized by others at the very time they most need support from others" (R 387 at 1-2). Thus, some patients pay the price of what benefits are available from orthodox treatments in order not to be abandoned by family and friends—"a psychological analogue to the theological concept of being 'cast into Hell' \* \* \*" (id. at 2). In many cases, it is family and friends who, amplifying the patient's feelings, try to get their anger and panic under control by manipulating the patient into use of medically unacceptable remedies. (See id. at 2.) The families of cancer patients, particularly parents of children with cancer, are understandably desperate for anything that will cure cancer. They often are beset by irrational feelings of guilt, and seek to assuage these feelings with the assurance that " \* \* \* 'we did everything for our child' even to the point of foolishness in going after an unproven cure \* \* \*" (R 394 at 2).

The shared responsibility of the loved ones of cancer patients for the patients' involvement with Lae-

trile for other unproven remedies) helps to explain why these families have been among the most vociferous proponents of Laetrile. "This reaction can be understood because such persons, whether they are family members or friends, have to justify the deceased's use of Laetrile by suggesting that the patients were considerably helped by the drug, that their lives were prolonged to a significant extent, or, at the least, that they did not suffer a great deal of pain during treatment with the drug. To do otherwise would require them to acknowledge that they made a mistake and misled the patients or that they went along with decisions which were clearly erroneous. Living with that kind of guilt is very difficult and the advocacy of Laetrile is a way of avoiding it" (R 433 at ¶ 15). It is only those family members who did not participate in, or dissented from, the decision to use Laetrile who, after the patient's death, raise their voices against the drug's use (see, e.g., R 47; R 429; R 300; R 348).

### 3. *Methods of Promotion of Laetrile*

As is obvious from the above discussion, the cancer victim and his or her family are extremely vulnerable to the kind of persuasion used so skillfully by Laetrile's promoters. This persuasion may take the form of highly polished and thus convincing films and books (see Tr. at 331) or of personal visits. The fact that many persons involved in Laetrile promotion believe strongly in the drug makes their presenta-

tions, because sincere, all the more compelling. In his affidavit, one cancer patient, speaking from his own experience, stated that "immediately after a diagnosis of cancer, most patients and family members are susceptible to something such as Laetrile, which offers a painless treatment with certain results" (R 388 at 2). The patient also stated that, somehow, the names of cancer patients in his area had been obtained by certain persons helping to spread the Laetrile theory. He indicated that Laetrile proponents exerted constant pressure on him and his wife to quit orthodox medical treatment and try Laetrile. Testimonials from patients who spoke in glowing terms of their recovery or successful treatment with Laetrile were offered to support the proponents' claim (id.). Laetrile promoters are diligent in searching out persons with reported cancer to offer their product. One physician noted that he had a patient who, within 24 hours of his being diagnosed as having lung cancer, received information in the mail telling him he ought to take Laetrile and where and how to get it (Tr. at 184).

Laetrile proponents are keenly aware of the involvement of family members and friends in decisions to accept unproven remedies and actively seek to persuade them of the drug's benefits. One woman who had had surgery and chemotherapy for treatment of breast cancer commented: "My biggest problem has been coping with well-meaning relatives and friends who swallow this propaganda of unprofessionals and



then try to make me feel guilty because I don't take their advice \* \* \*" (R 96).

Laetrile proponents play upon the victim's frustration with a medical establishment that cannot offer the certainty of a cure. Some patients reportedly turn to Laetrile precisely because it is "illegitimate," behavior that appears to be "an anger reaction toward legitimate medicine" (R 387 at 3). This antagonism toward the medical establishment is fanned by Laetrile proponents (as it has been by the purveyors of previous "unproven" remedies) to a pitch that most observers would consider absurd. When a speaker at the oral argument asked the audience, which consisted predominantly of Laetrile supporters, if "you really think that a quarter of a million physicians across the country can let people die because they want to make a profit off of them?", the audience response was a loud chorus: "Yes" (Tr. at 191).

Laetrile proponents also play upon and build the cancer patient's fear of legitimate cancer therapies. (See R 421 at 2: "The promise of a painless cure through Laetrile, as opposed to orthodox medical methods with their side effects capitalizes on the fear of pain and suffering".) "Slash (or cut), burn, and poison" are the code words of the Laetrile supporters for the proven remedies of surgery, radiation and chemotherapy (see, e.g., Tr. at 291, 357, 463). A videotape of an interview with a cancer patient (R 419, Ex. B; see also R 197 at ¶ 7) that is part of the record shows graphically the costs of this sort of

propaganda. The victim is a women who, at the time her breast cancer was discovered, was given a reasonably good prognosis of recovery after surgery. Out of fear of surgery she tried Laetrile therapy. Though the tumor grew to involve her whole breast she continued to avoid conventional therapy, even trying, after Laetrile did not help, an "asparagus" diet cure, garlic, and finally a fruit and vegetable diet with hot baths. When, nearly at death's door, she returned to the surgeon, it was too late for surgery to be effective. She then was convinced to try radiation therapy, which she testified she had avoided because the negative descriptions of it in Prevention magazine, to which she had long subscribed. The radiation therapy helped reduce the size of her tumor and make her more comfortable, but her expected survival was greatly diminished by her delay in obtaining effective treatment. This kind of disparagement of conventional therapy, a bulwark of the campaigns of Laetrile proponents, is perhaps the most morally reprehensible aspect of the pattern of the drug's promotion.

#### *4. The Sampson Survey*

While the conclusions about the reasons for use of Laetrile expressed in the record are based upon a multitude of experiences by various witnesses with patients taking Laetrile, it is interesting to note the conclusions of the one attempt to survey Laetrile patients about their reasons for using the drug.

Based upon about 20 interviews with cancer patients who abandoned orthodox therapy in favor of Laetrile, Dr. Wallace I. Sampson, Clinical Associate Professor of Medicine, Stanford University School of Medicine, stated that about 75 percent of the patients reported that they had serious problems with their physicians. About 75 percent believed in Laetrile's therapeutic rationale and effectiveness. About 75 percent of the patients were involved in other methods of therapy that included high doses of Vitamin C, megavitamin therapy, and immunotherapy given by unqualified individuals. Dr. Sampson is of the opinion that the patients receiving Laetrile were involved in other types of unorthodox therapy because of their outlook on life (i.e., they seek non-rational, magical solutions to the problems of dread and often incurable illness) or perhaps because of difficulties in relating to a standard physician. A large majority of the patients believed that there is a conspiracy to keep Laetrile off the market. Less than 10 percent of the patients tried to inform themselves about Laetrile from non-Laetrile sources. (See Tr. at 118-119; R 398 at 4.)

#### C. THE LAETRILE TESTIMONIALS

Unproven cancer remedies like Laetrile are invariably supported by numerous testimonials of persons who pronounce themselves satisfied with the results they, or their deceased friends and relatives, have achieved with the drug. The present widespread use of Laetrile as an alternative to remedies of proven

effectiveness illustrates the problems to which such "evidence" of a drug's effectiveness leads, and it is a legitimate question to ask why there are so many such testimonials.

The Commissioner does not doubt the honesty or the sincerity of the many testimonials for Laetrile, but many of the positive experiences reported may be accounted for by explanations other than the claimed effectiveness of the drug. The placebo effect discussed above undoubtedly accounts for some of the reports, particularly those claiming decrease in pain and increased sense of well-being. Experts interested in the question have provided other explanations. Most of the patients reporting Laetrile "cures" appear actually to have had the benefit of other, proven effective therapies. Some of those who believe themselves cured may never have had cancer at all. Others may simply not be cured, despite their belief.

Many of the testimonials and anecdotes concerning the effectiveness of Laetrile replay the same scenario. The cancer patient is told he has cancer and agrees to surgery, radiation, and/or chemotherapy. After some time, the patient, feeling nauseous, weak, and general malaise, in desperation turns to Laetrile. Within a few days or weeks after stopping orthodox treatment and starting to use Laetrile, the patient feels better, has an appetite, and is able to move about on his own. The patient in all sincerity attributes his recovery and feeling of well-being to his decision to reject orthodox medical treatment and to choose Laetrile. (See, e.g., R 9; R 35; R 223; R 267;

R 315; R 391; R 483.) Many families of deceased cancer patients who had orthodox therapy and who then used Laetrile believe that the patient benefited from the Laetrile and might still be alive if they had turned to Laetrile earlier. (See, e.g., R 19; R 208; R 279.)

It is easy to understand how such a situation could develop. A doctor may prescribe 10 applications of a proven cancer drug, perhaps after surgery. The cancer may have been totally removed by the surgery or it may have been totally destroyed by, for instance, the 7th of the 10 applications of the effective drug. Because the physician cannot know this, and because he cannot risk the chance that some cancer remains, he has prescribed the recognized treatment regimen. Use of cancer drugs (referred to as chemotherapy) or of radiation may involve unpleasant side effects. The patient, sickened by the side effects of the drug and importuned by Laetrile proponents, may stop the chemotherapy before the prescribed regimen is completed. As the side effects clear up, the patient feels better. If a full cure has been accomplished, it will be attributed to Laetrile. If it has not, the surviving family may well believe that, since the patient felt better after stopping chemotherapy and starting Laetrile, the therapy was only received "too late." See R 184 at ¶ 7:

Testimonials attesting to a feeling of general improvement and cessation of pain in patients upon abandonment of radiation and chemotherapy in favor of Laetrile treatment do not indi-

cate that Laetrile is effective in curing cancer or in relieving pain. The feeling of well being experienced by these patients derives from two phenomena, one physical and the other psychological. Chemotherapy and radiation treatments produce unpleasant side effects in most patients. When such therapies are stopped, the side effects they produce disappear. This natural physical effect in the case of these patients is reinforced when Laetrile is administered because of the patients' expectation that the treatment will have a beneficial effect.

Dr. John A. Richardson, himself a major proponent of Laetrile therapy, stated that 85 percent of the 4,000 to 5,000 patients treated with Laetrile at his clinic had previously received some type of orthodox medical treatment (Tr. at 463).

Sometimes conventional and Laetrile therapies are administered simultaneously, with any beneficial effects attributed by patients to the latter. Dr. Emil J. Frereich is involved in the development of cancer drugs. He stated that:

(W)e have numerous patients who are receiving developmental therapy drugs which have at the time, real promise, and subsequently prove to be useful and are introduced into practice, who unbeknownst to us, were also taking therapy with laetrile and when their disease responds to therapy, (they) inadvertently ascribe it to the effectiveness of the unproven remedy, whose administration is revealed to us subsequently. When we compare the responses of patients on a given



therapy who have received laetrile at the same time, with those who received none, there is no significant difference, which indicates clearly that those observed responses were due to the cancer chemotherapy drugs which were being administered by us and not by the additional use of laetrile (R 390 at ¶ 20.)

For other testimony on the propriety of attributing to Laetrile cures that may be caused by other, proven effective, drugs, see, generally, R 174 at ¶ 9 and R 185, at ¶ 20e.

"Some people who believe that Laetrile cured them never had cancer to begin with" (R 174 ¶ 9). In a number of the "case histories" submitted to show Laetrile's effectiveness, there is no acceptable showing that the patient ever had cancer. (See, e.g., R 183, Att. 16, App. 2; R 184, Ex. 2; R 378, Att. "Supplementary Report," cf. evaluation of case histories above.)

In one 1955 pamphlet, Dr. Krebs, Sr., discouraged biopsy, the procedure often used to determine whether a tumor is malignant (cancerous) (R 183, Att. 7 at 14). He urged instead that a special urine test, not generally accepted by the medical community as useful, be the means for diagnosing cancer (id. at 16). Even where the diagnosis has been done by someone other than a Laetrile proponent, a mistake is possible. Some cancers which are discussed in reference to Laetrile are very difficult to diagnose histologically. Thus, a diagnosis of cancer may often on later review be reversed. (See Tr. at 141.)

"Many cancer patients have given testimonials believing themselves cured, only to discover later that they still have the disease" (R 174 at ¶ 9) Since he is involved in the testing of cancer drugs, Dr. Emil J. Freireich is in a good position to follow up on patients who leave his program to use Laetrile. Dr. Freireich reports that "(i)n virtually every instance, (Laetrile patients treated in our department and subsequently followed by our tumor registry, have been) found to have evidence, not only of progressive disease, but to have expired after receiving such unsuccessful treatment, and a significant fraction eventually return to our clinic for more developmental therapy" (R 390 at ¶ 20).

An illustration of what, in all likelihood, explains most Laetrile testimonials appears in the record:

Testimonials fail to provide objective evidence that there has been control or regression of a tumor which is attributable to the use of Laetrile \* \* \*. To illustrate why such data are important, let us examine two typical versions of testimonials from women who state that their cancer of the breast was cured by Laetrile. The first testimonial is from Jane Doe. She discovered a lump in her breast and based upon the urging of friends has consumed on her own initiative a number of Laetrile tablets. It is also possible that she saw a doctor who administered injections and prescribed a special diet. In a month, the lump has disappeared, and Jane Doe sings the praises of Laetrile. "It cured my cancer; I am living proof." This is not credible

evidence. The lump detected may have been caused by a variety of conditions. Without laboratory confirmation that a malignant condition existed, there is no basis to assume that it was cancer and that Laetrile contributed to its disappearance. The second testimonial is from Dorothy Doe. She had objectively diagnosed cancer, underwent a mastectomy and postoperative chemotherapy or radiation treatments. The physician informs Dorothy that an additional surgical procedure may be necessary. Dorothy decides against further unpleasant treatment and takes Laetrile. Now, six months or three years later—time makes little difference—she, too, sings the praises of Laetrile. Dorothy's experience does not constitute evidence. It is possible that her orthodox treatment was successful; it is possible that she still has cancer, but that it will not manifest itself for another year or, indeed, as is sometimes the case, for another dozen years. The point is that there are no objective data upon which to assess Dorothy's condition at the time Laetrile was administered and the effects of Laetrile. In the absence of such data, there is no basis for a claim that Laetrile was effective (R 191 at ¶ 14).

As another affidavit states,

\* \* \* It is a certainty that any substance without significant toxic or harmful effect, including mystical activities, faith healing and all other types of non-toxic or non-harmful remedies will be effective in a small fraction of the very large population of patients with hopeless terminal cancer. Those individuals who fail to respond

to such treatment, that is, who have the expected outcome, which is progression of their cancer and death, are no longer living and those rare individuals who have the exceptional or miraculous outcomes frequently live for long periods of time. It is obvious that a large number of individuals can be identified who have unusual outcomes. These individuals are of course easily convinced of the effectiveness of such treatments and are free to testify to their effectiveness for as long as their disease remains in control. Such testimonials contribute no significance toward our understanding of the effectiveness of any treatment for cancer. Evidence accumulated in the proven, objective, medical and scientific fashion is the only evidence that can be of use in evaluating the potential of any treatment for influencing the course of malignant disease (R 390 at ¶ 21).

Dr. Melvin Krant, Professor of Medicine and Psychiatry and Director of Cancer Programs at the University of Massachusetts Medical Center, reviewed a number of the testimonials submitted to the record from patients and relatives and friends of patients who have been treated with Laetrile. He stated that the testimonials "do not offer evidence for effectiveness because frequently the treatments with Laetrile were taken after other treatments such as surgery, radiation, or chemotherapy. At times, the Laetrile was taken in conjunction with other modes of therapy such as chemotherapy. In such instances, it is impossible to know whether the Laetrile added anything to the patient's response. There are no objec-

tive ways to measure the patient's response. In many instances, it seems like the main emphasis of the testimonials is on the patient's emotional reaction to being treated. Because the testimonials are not presented in a scientific manner, it is also impossible to determine if there were any side effects from Laetrile administration" (R 453 at 1-2).

## V. OTHER ISSUES REGARDING LAETRILE

### A. USE OF LAETRILE OUTSIDE THE UNITED STATES

Laetrile's proponents have sometimes sought to give the impression that Laetrile is in use around the world and that it is only the United States' overly restrictive drug laws or an evil conspiracy among drug companies, physicians, and bureaucrats that is preventing marketing of the drug in this country. (See, e.g., the claim, in a 1963 publication. *Control for Cancer* by Glenn D. Kittler, that Laetrile was being studied in several countries in addition to the United States: Canada, the Philippines, Japan, England, Belgium, Italy, Union of South Africa, and Mexico (R 318 at 31.) The book also reported that the drug was registered in Iran in 1962 (*id.*). (See also the reference to the use of Laetrile (or Amygdalin) in West Germany in the late 1960's (R 302, Ex. G).) (Cf. R 198, Ex. 2 at 24, (transcript of film *World Without Cancer*); Tr. at 424.)

The record reflects no international recognition or use of the drug. The State Department and the

United States Mission to the World Health Organization made an effort to determine whether Laetrile, Amygdalin, Vitamin B-17, or such drug under any other name was known and approved elsewhere in the world. The State Department sent inquiries to all American embassies instructing embassy officials to ascertain the status of the drug in their respective host countries, and the mission to the World Health Organization made telephone inquiries of member states throughout Western Europe. The following information was obtained:

The American Embassy in Mexico advised that in 1974 the Mexican government gave provisional approval, contingent upon the presentation of evidence of Laetrile's effectiveness in treating cancer, to two laboratories in that country to manufacture the drug. This approval was cancelled in late 1976 because no positive results were obtained in research carried out at the Medical Center General Hospital. The decision to ban Laetrile has been appealed by Laetrile proponents and is now in the Mexican courts (R. 426; see also Tr. at 430).

The mission to the World Health Organization had been told by some European contacts that "Laetrile" can be "purchased across the counter in Geneva without prescription" (R 426). The American Embassy in Switzerland, upon inquiry, was told that Laetrile is not sold on the Swiss market and is not approved there. One company does sell "small quantities of Laetrile," "exclusively to cancer research scientists" primarily in Western Europe. The company told the



American embassy in Bern that "Laetrile is not made available commercially, nor is it sold as a cancer 'cure'" (id.).

In Madagascar, Laetrile is known as Amygdalin and is considered a poison by health authorities. Its use is prohibited. In Chile, Laetrile is also known as azaribina and its use is prohibited under any circumstance. This prohibition followed receipt of Newsletter 172 from the World Health Organization which described the potential dangers of use of the drug. The importation or use of Laetrile (Amygdalin) is illegal in the Republic of Korea (id.).

Health officials in Guyana reported that Laetrile has been used there. The Minister of Health indicated that he was not aware of FDA's prohibition of the use of Laetrile, however, and that, since the United States' standards are closely followed in that country, his country would also ban the drug (R 426).

The State Department inquiry drew 69 responses from around the world. Each of the countries not already mentioned responded by indicating that "Laetrile," "Amygdalin," and "Vitamin B-17" were unknown or were not approved for use for treating cancer or any other use. The responding countries included the Philippines, Japan, the United Kingdom, Belgium, Italy, South Africa, and the Republic of Germany, as well as France, Korea, Taiwan, Hong Kong, India, and others from every part of the globe (id.). The United States Mission at the World Health Organization confirmed that Laetrile "is not regis-

tered and by definition, unavailable," in any of WHO's member states throughout western Europe (id.).

#### B. CLAIMS THAT LAETRILE IS A VITAMIN OR FOOD

Proponents of Laetrile (or amygdalin) have in recent years contended that their product is a vitamin or that it is a natural food substance rather than a drug. These claims are properly irrelevant to the questions this administrative proceeding was intended to address. However, in light of the interest in the vitamin issue demonstrated by the submissions to the record, the Commissioner will take this opportunity to discuss it. The potential safety problems presented by this concept will also be discussed.

##### 1. *A Vitamin or Food May Be a Drug As Well*

This question is irrelevant to the issues in this administrative proceeding because, even if Laetrile (or amygdalin or "laetrile") were a vitamin (or a food), it would still be a drug. Any substance, including a vitamin or food, is a drug and subject to regulation as such if it is intended for use in the "diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals \* \* \*" (21 U.S.C. 321(g) (1)). (See *Rutherford v. United States*, *supra*, 542 F.2d at 1140; *United States v. General Research Laboratories*, 397 F. Supp. 197, 200 (C.D. Cal. 1975).<sup>7</sup>

<sup>7</sup> Section 411 of the act (21 U.S.C. 350) deals specifically with vitamins and minerals. Section 411(a) (1) (B) does limit

As the previous discussion illustrates, there is no question that Laetrile or amygdalin has been recommended in the treatment of cancer. In fact, in the very article in which Ernst T. Krebs, Jr., explained his theory that his product was "Vitamin B-17", he promoted it for cancer treatment. (See R 183, Att. 10c.)

It has been suggested that the claims that Laetrile (or amygdalin) is a vitamin or a food are simply an effort to establish that the substance is covered by the food requirements of the Federal Food, Drug, and Cosmetic Act and its regulations rather than those requirements applied to drugs. (See, generally, Tr. at 216, 225, 405; R 173, Att. "Questions most frequently asked about 'Laetrile,'" at 1; R 416 at ¶ 16.) One court has called the attempts by Laetrile proponents to represent Laetrile as something other than a drug, "a patently absurd and transparent attempt

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the authority of the Secretary to classify a vitamin as a drug "solely because it exceeds the level of potency which the Secretary determines is nutritionally rational or useful." The vitamin provisions do not, however, affect FDA's authority to classify and regulate vitamins as drugs if they are represented to be for use in the diagnosis, cure, mitigation, treatment, or prevention of disease. The conference committee report states, "Except as specifically provided, the conference substitute does not alter the drug or food provisions of the Federal Food, Drug, and Cosmetic Act. If a product containing vitamins, minerals or other ingredients is a drug within the meaning of Section 201 (g) of the Act, the Secretary may, with regard to such product, exercise his authority under Chapter V of the Act" H. R. Rep. No. 1005, 94th Cong. 2d Sess. (April 2, 1976); (see also, 122 Cong. Rec. H3244-H3248, April 12, 1976).

to avoid the drug labeling provisions of the Federal Food, Drug, and Cosmetic Act." *United States v. Spectro Foods Corp.*, Civil No. 76-101 (D.N.J., Jan. 29, 1976) (R 173, Att.). The Commissioner does not agree that Laetrile is a vitamin. (See discussion below.) It is clear, however, that even if Laetrile were a vitamin (or a food) it would be subject to the drug provisions of the act.

## 2. *Is Laetrile a Vitamin?*

This administrative proceeding was not intended to address the issue of whether Laetrile is a vitamin, and testimony on that issue was not solicited. Nevertheless, a considerable amount of evidence in the record addresses this issue. It appears that (a) Laetrile proponents classify amygdalin and certain related substances as a vitamin under their own definition of that term and (b) experts in the vitamin area, utilizing the criteria against which each of the legitimate vitamins have been assessed, conclude that amygdalin and other nitrilosides are not a vitamin.

(a) *Proponents' Claims.*—The idea that Laetrile could be considered a vitamin first appears in a pamphlet,\* in use in 1965, published by Krebs Laboratories and entitled "Cancer Is A Deficiency Disease:

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\* The Krebs were no strangers to the "vitamin" area. Ernst T. Krebs, Jr.'s, marketing of another of his inventions, "Vitamin B-15" ("pangamic acid"), led to his plea of guilty to a charge of causing the introduction into interstate commerce of an unapproved new drug in 1962 (R 185, Att. 16, App. 17 at 7).

The Deficiency of Cyanide Sugars" (R 201, Ex. C, No. IV). In that pamphlet, amygdalin and other "cyanogenetic glucosides" are characterized as pro-vitamins for vitamin B-12. This means that they participate in the formation of vitamin B-12. It is stated that "during the process of formation the liver is thoroughly fumigated and rendered sterile (id.). The real anticancer effect of amygdalin is said to be not this formation but the release of cyanide in the cancer cells by the mechanism discussed above under "Theories of Action." It is interesting to note that another Laetrile proponent, Dr. Navarro of the Philippines, states that vitamin B-12 should never be administered to cancer patients (R 318 at 165).

The pro-vitamin theory had apparently been set aside by 1970 when an article by Ernst T. Krebs, Jr., referred to previously, "The Nitrilosides (Vitamin B-17—Their Nature, Occurrence and Metabolic Significance (Antineoplastic Vitamin B-17))," was published (R 183, Att. 10c). In this article, Krebs, Jr., uses the term "vitamin B-17 (nitriloside)" as "a designation proposed to include a large group of water-soluble, essentially non-toxic, sugary compounds found in over 800 plants, many of which are edible" (id. at 75). He indicates that the compounds "are collectively known chemically as beta-cyanophoric glycosides. They comprise molecules made of sugar, hydrogen cyanide, a benzene ring or an acetone" (id.). These compounds could be hydrolyzed by beta-glucosides to a sugar, free hydrogen cyanide, and benzaldehyde or acetone (id.). He states that amygd-

daline is one of the most common of the nitrilosides and that it "occurs in the kernels or seeds of practically all fruits" (id.).

Mr. Krebs, Jr., in this article, attempts to build a theory that vitamin B-17 is a specific dietary factor that could be used to prevent and to cure cancer. He explains that prevention and cure occur through the cytotoxic (toxic to cells) compounds of vitamin B-17—hydrogen cyanide and benzaldehyde—through mechanisms discussed elsewhere in this opinion (id. at 80). He concludes that: "In nitriloside or vitamin B-17 we have a new vitamin in which all of us are severely deficient" (id. at 84). The theory that Laetrile (or laetriles) constitutes a vitamin has found another proponent in the person of Dr. Dean Burk, a biochemist and president of the Dean Burk Foundation, Inc. (see, generally, R 302; Tr. at 401 et seq.).

Clearly, whether or not a given substance comes within the definition of vitamin depends upon the definition chosen. In his affidavit, Burk defines a vitamin as a substance which is "virtually non-toxic, water-soluble, an exogenous nutrient or food factor, and active in relatively small, essentially catalytic, non-caloric amounts, and is essential or beneficial in normal metabolism and/or physiologic functioning to *overcome deficiency lesions and symptoms of nutritional disease*" (emphasis in original) (R 302 at 4). Dr. Burk continues that in animal experimentation " \* \* \* the deficiency lesions and symptoms of nutritional disease are best illustrated by the action of amygdalin in lengthening of ani-



mal lifetime or decreasing development of metastases, or both, and increase in health and well-being \* \* \*” (id.). (See also Tr. at 408 and 465.)

Thus, even by the Burk definition, the claim that Laetrile is a vitamin depends in large part on the substance’s ability to combat cancer, an ability not shown by testing convincing to drug experts in general. Proponents of the vitamin theory claim that the higher the everyday diet is in nitrilosides, the lower the incidence of cancer (R 73 at 36). Others claim that it may not be only high nitriloxide levels that account for this observation but that other dietary elements (e.g., vitamin C) may play a role. (See, generally, R 318). These claims are based upon assertions that in some geographical areas, where the normal diet contains nitrilosides in abundance, cancer does not exist. Evaluation of the prevalence of cancers requires careful studies by competent epidemiologists and suitable cancer registries, which contain reports by professional pathologists (R 399 at ¶ 9). What evidence does exist in this area indicates a complete lack of the correlation between high nitriloxide diet and low cancer incidence that the Vitamin B-17 proponents claim. The record contains citations to numerous reports showing that a variety of cancers do occur in populations consuming nitriloxide-containing diets. These include findings that cases of most of the recognized cancers appear in the Kampala Cancer Registry, Uganda (id.). There are also references to published papers from the Ibadon Cancer Registry, Nigeria on Burkitt’s lymphosarcoma, Kaposi sarcoma and breast cancer, cancer of the

bladder in Kenya, and the cancer incidence in Bantu (id.). Some cancers that are rare or absent in North America and Western Europe occur in the populations which consume high levels of nitrilosides (id.).

In the film “World Without Cancer,” the people of the Kingdom of Hunza in the Himalayan mountains are said to eat a diet containing over two hundred times more nitrilosides than the average American diet and to prize above all other foods the apricot seed. It is stated that “[v]isiting medical teams from the outside world report that there never has been a case of cancer in Hunza” (R 198, Ex. 2 at 3). However, in 1955, a Japanese medical expedition studied the Hunza people and reported that they have many diseases, including cancer (R 173, Att. “Questions Most Frequently Asked” No. 6; Tr. at 338).

Similarly, the film claims that the Eskimos eat a high nitriloxide diet and are “found to be totally free of cancer” (R 198, Ex. 2 at 8). The Eskimos have also been found to have cancer (R 173, Att. “Questions Most Frequently Asked” No. 6; Tr. at 339). In commenting on another reference to “the diets of the cancer-free population” (R 217 at 2), Thomas H. Jukes, Ph.D., states correctly: “There are no cancer-free populations” (R 416 at ¶ 28(C)).

(b) *Vitamin Experts’ Position.*—Numerous nutrition experts and organizations concerned with nutritional science provide support in the record for the Commissioner’s conclusions that “Laetrile,” or “amygdalin,” or “nitriloxide,” is not a nutrient or vitamin. (See, e.g., R 173, Att. “Questions Most

Frequently Asked" (American Cancer Society); R 168, Att. "The Vitamin Fraud" and R 399 at ¶ 12(C) (David M. Greenberg, Ph.D.); R 416 (Thomas H. Jukes, Ph.D.); R 378. Att. Editorial; Att. American Institute of Nutrition letter; R 169 at ¶ 17 (Vincent T. DeVita, Jr., M.D.); R 191 at ¶ 11 (Philip S. Schein, M.D.); R 227 at 3 (National Council on Drugs).) The steps which are necessary to establish that a substance is a vitamin are described in the record. These steps include the publication in reputable journals of a complete description of the research procedures, and confirmation, by other scientists, of the results obtained. If the work cannot be repeated, the existence of the vitamin is not recognized (see R 416 at ¶ 15). Additional steps include demonstrating the presence of the purported vitamin in foods, determination of its exact chemical molecular structure, the demonstration of its effectiveness, and its chemical synthesis. After these steps are completed, the Food and Nutrition Board of the National Academy of Sciences sets up Recommended Daily Allowances for the vitamin which then must be adopted by the Food and Drug Administration (id.).

The lack of scientific evidence of any effect, which has prevented Laetrile from being recognized by experts as a safe and effective drug, also prevents recognition of its claimed status as a vitamin. (See e.g., R 416 at ¶ 16: "(T)here are no data available to show that a disease state is produced or alleviated by the exclusion from (or) addition to the diet of amygdalin".) Other experts emphasize that there is no

evidence that (1) laetriles (*beta*-cyanogenic glucosides, vitamin B-17) are essential nutritional components nor that (2) they promote any physiological process vital to the existence of any living organism. (See R 168, Att. at 347; R 395.)

A compelling point made by experts in this area is that if there were a vitamin B-17, and if cancer were a vitamin B-17 deficiency disease, then every animal deprived of the vitamin would get cancer while no animal given the vitamin in sufficient amounts would get cancer. It is noted, that "No person given adequate vitamin C, for example, ever gets scurvy" (R 198 at 5). Stated another way: "The key to the term 'vitamin' is that the absence of vitamins from the diet in an experimental animal or a human being must lead to the appearance of a nutritional deficiency disease, which is prevented or cured by adding the vitamin to the diet. Laetrile has no such property" (R 416 at ¶ 14).

It is further stated that "(no vitamin has) the property of destroying tissue, such as cancer tissue, that is claimed of Laetrile. Such a property would be incompatible with the action of vitamins" (Tr. at 223). Other experts in this area rejected the claimed vitamin status in part on the grounds, discussed below, that amygdalin is, or can be, harmful to the body. It is pointed out that, amygdalin properly belongs to the class of compounds termed "toxicants occurring naturally in foods". (R 416 at ¶ 27(A) (1)).

### 3. Dangers of Ingestion of "Vitamin B-17"

As has been demonstrated above, the presence of *beta*-glucosidase, oxynitralase, and amygdalin together in apricot pits presents the potential for a combination that would release cyanide and cause poisoning of the individual consuming an extract of the pits. Additionally, though *beta*-glucosidase is not present in animal tissues, it, and other substances capable of breaking down amygdalin, may be present in the digestive track and thus may break down orally consumed amygdalin to release cyanide in the body. It is therefore with great concern that the Commissioner views the emergence of the theory that human beings should step up their consumption of "naturally occurring" nitrilosides such as amygdalin.

In his vitamin B-17 article, Ernst T. Krebs, Jr., notes that while the "stupidity" of "political power" may keep prepared vitamin B-17 off the market, six or seven teaspoonsful of defatted apricot seed or kernel would supply what is considered to be an adequate oral dose of nitrilosides (R 183, Att. 10c at 84). He suggested, "It is best that the *beta*-glucosidase enzyme be completely heat inactivated in such material" (id.). He does not indicate how much heat inactivation should be accomplished, nor does he cite any support for the idea that it can be.

There are documented cases of poisoning, some fatal, due to the consumption of apricot pits or kernels. The toxic element in these cases is the hydrogen cyanide which is released from the cyanogenetic glu-

cosides by the action of the enzymes (including *beta*-glucosidase) present in apricot kernels (R 378, Att. "California Morbidity Reports," Att. "Hazards to Health"). The suggestion by Mr. Krebs, Jr., that the *beta*-glucosidase be "inactivated" can be taken as tacit—too tacit—acknowledgement that the kernels and/or pits present a hazard when consumed unless the enzymes are first destroyed. The Commissioner notes that other proponents of Laetrile clearly state that amygdalin products should never be given by mouth because the hydrochloric acid in the stomach is capable of hydrolyzing the drug (R 318 at 158). A 1954 document, "The Rationale and Clinical Evaluation of Laetrile-Beta-Glucosidase Palliative Therapy" states, "CAUTION: Laetrile (1-mandelonitrile-*beta*-glucuronidase) is NOT TO BE TAKEN ORALLY. It is extremely toxic by this route of administration, since the gastric hydrochloric acid acts to hydrolyze the glucoside with the release of hydrogen cyanide" (R 388, Ex. 5).

Dr. Burk seeks to support the idea that Laetrile or amygdalin is a food and, among other things, may be safely consumed by an allegation that "\* \* \* laetrile is listed in the HEW-FDA GRAS list (foods 'Generally Regarded (sic) as Safe') under the heading of natural extractive from bitter almond, apricot or peach kernels" (R 302 at 3; see also Ex. B). The material to which Dr. Burk refers is "Bitter almond (free from prussic acid)" which does appear on the generally recognized as safe (GRAS) list, 21 CFR



182.20. (Prussic acid is another name for hydrogen cyanide.) The material on the GRAS list, however, is an oil extracted from peach, almond, or apricot kernels. After cold pressing the oil from its source, it is processed to effect enzymatic hydrolysis of amigdalín. There is no amygdalín present after the hydrolysis step. The final product is essentially benzaldehyde. "Thus the material listed for flavor use \* \* \* is not amgydalín and thus neither is it Laetrile" (R 415 at 2). Dr. Burk's contention is thus incorrect and has no basis in fact.

The idea that foods containing nitrilosides may be safely consumed is also supported by stories of "nontoxic" nature of nitrilosides which are found in the diets of various peoples. This claimed nontoxicity is not borne out by reality. In some parts of Africa two important human diseases—human ataxic neuropathy and endemic goitre—appear to be associated with high cassava intake (R 183, Att. 20 at 161; R 378, Att. 6). (Cassava contains linamarin, a commonly consumed nitrilósíde (R 217, Att. "Sickle Cell Anemia" at 51). It is also reported that cows have been killed by eating large amounts of young millet, which is particularly high in nitrilosides, and intoxication of other animals has been reported. (See R 416, Ex. 5 at 302.) There have been reports in this country of toxicity and, in some cases fatalities, in humans from consumption of amygdalín-containing substances (See, e.g., R 378, Att. "California Moribidity"; see also R 378, Att. "Hazards to Health; Cyanide Poisoning from Apricot Seeds Among Children in Central

Turkey," Sayer et al.). Thus there is ample and clear indication that the consumption of "nitrilosides" is not without hazard. To urge the public to consume "apricot pit milkshakes" or similar foods in order to be sure to get an ample supply of amygdalín or "vitamin B-17" or "nitrilosides" is irresponsible and foolhardy.

#### C. FREEDOM OF CHOICE

The administrative record contains many comments not directed to the legal issues of Laetrile's "new drug" or "grandfather" status or even to the question of whether the drug is safe or effective for use in cancer therapy. Rather these comments support the proposition that a person should be free to choose his or her own cancer therapy, at least if the drugs involved are not overtly toxic (see, e.g., Tr. at 33; R 231; R 238; R 242; R 209; R 211; R 283; R 500; R 155; R 272). The issue of "freedom of choice" is irrelevant to the issues remanded to the agency by the Rutherford courts. Nevertheless, because of the demonstrated public interest in this issue, the Commissioner has given it, and submissions addressing it, careful consideration.

The very act of forming a government, of course, necessarily involves the yielding of some freedoms in order to obtain others. In passing the 1962 Amendments of the act—the amendments that require that a drug be proved effective before it may be marketed—Congress indicated its conclusions that the absolute

freedom to choose an ineffective drug was properly surrendered in exchange for the freedom from the danger to each person's health and well-being from the sale and use of worthless drugs. This is in fact the same decision made by those in government who have decided over the years that only those persons may practice medicine who have been certified by experts to be qualified to actually help the patients who would choose to seek their assistance.

Some would argue that the lawmakers' well-considered decision to prohibit the use of drugs not shown to be effective was the wrong one. One alternative suggested is that a drug such as Laetrile should be marketed with labeling which indicates that experts do not consider it to be effective. The present use of Laetrile vividly illustrates the impracticability of such a solution. There can be few patients taking Laetrile in this country today who do not know that the government and most experts consider it worthless. Yet the drug continues to be used, to the detriment of cancer patients who might otherwise be helped by conventional treatment.

The choice to use Laetrile is seldom, in any case, a free one. As the discussion above (Why Do People Use Laetrile?) illustrates, a cancer patient is a person beset by immense stresses, physical, psychological, emotional and societal; and the persuasion that the patient and his family are subjected to by Laetrile proponents is seldom limited to a rational laying out of competing arguments. The information that the proponents of Laetrile provide is false—that the drug

cures, palliates, relieves pain, "controls" cancer. As Dr. Sampson's survey, discussed above, indicates, few Laetrile patients make an effort to hear the argument against Laetrile therapy. The idea that a reasoned free choice is involved in the selection of Laetrile rather than legitimate therapy is thus ultimately an illusion. (See R 421 at 1.)

The record contains the views of many persons who have considered the issue of "freedom of choice" in cancer therapy. Each represents a thoughtful attempt to deal with this question, which, while irrelevant to the legal issues which are the subject of this opinion, is troubling to those concerned with the Laetrile problem. These comments may be grouped roughly as supporting the two responses to the "freedom of choice" argument set forth above: (1) The surrender of an absolute freedom to choose among cancer remedies in order to obtain the greater freedom from the suffering associated with use of ineffective remedies is a rational decision; and (2) the "choice" of unproven cancer remedies cannot fairly be characterized as "free."

#### 1. *Balancing Freedoms*

Reverend Allan W. Reed, Director, Department of Pastoral Services and School for Pastoral Care, Massachusetts General Hospital, considered the ethical side of the "freedom of choice" question. He states "The ethical issues of a group of legislating for an individual, thereby threatening the principal (of) freedom of choice, contrasts with the ethical principal

of a government protecting its citizens from fraud and abuse. In the case of a drug for which there is no proven efficacy, the ethical weight is on the side of protection of the citizens" (R 148).

Leroy G. Kerney, Chief of the Department of Spiritual Ministry at the Clinical Center, National Institutes of Health, pointed out that, "Freedom of the individual is important. But when the freedom to accept any drug for treatment and the freedom to injure oneself collide, a judgment must be made: Stop signs or restrictions on turning at certain corners restrict my freedom in driving, but, at the same time, they protect my freedom from hurting myself and others in traffic" (R 414 at 3).

J. Philip Wogaman is Dean and Professor of Christian Social Ethics at the Wesley Theological Seminary and past president of the American Society of Christian Ethics. He noted an "initial presumption" in favor of freedom from governmental prohibition but concluded that Laetrile should be banned for three reasons: (1) The ban prevents fraud in the medical marketplace; (2) "[M]isrepresentation in the field of medicine is particularly serious because it undermines public confidence in medicines that are of real value"; (3) "(T)here is a real danger that persons may be led by false hopes in a worthless drug to neglect treatment at a time when it could be most effective" (R 417 at 2-3).

Dr. James F. Holland of the Mount Sinai School of Medicine points out that the freedom achieved by regulation of drug products is often the freedom to

live: "For the patient ignorant of the inertness of Laetrile as an anticancer drug, there is an overriding concern that he not be denied his individual freedom by untimely death from cancer from having relied on Laetrile to help. This is a cruel deprivation of individual freedom, since the patient does not get a second chance" (R 396 at 2).

James Harvey Young, Ph.D., a historian of health quackery, discussed the past use of the freedom of choice concept and phrased his conclusions concerning the validity of application of that concept to health care in colorful terms. He states that acceptance of the primacy of the freedom to choose medical therapies "leads only toward the license of those ancient days, when 'the toadstool millionaires,' preaching religion and spouting patriotism, operating without restraint, fleeced and often killed their gullible victims. That is a fate from which seven decades of constructive legislation, beginning with the Pure Food and Drugs Act of 1966, has somewhat rescued the nation. Complex, modern, industrial, urbanized society, with standards of medical judgment far more precise than those existing in the nineteenth century, cannot afford to let the nation's health concerns be governed by a distorted definition of that great symbol, 'freedom', which would return piratical anarchy to the realm of health" (R 400 at 11-12).

## 2. *The Choice Is Not Free*

The discussion above of "Why People Use Laetrile?" describes the many pressures that induce can-



cer patients and their families to make the decision to use Laetrile. Orville Eugene Kelly is a cancer patient who has founded an organization called "Make Today Count," which now has 103 chapters in 30 states, to help other cancer patients and their families deal with the problems that discovery of cancer entails. He addressed the question of "freedom of choice" in an affidavit submitted to the record (R 389). He notes from personal experience that patients and their families are often susceptible to arguments that a painless drug like Laetrile can cure them (*id.* at 2) and describes the persistence with which those arguments are made. He himself has tried to present the counter-arguments to other cancer patients. "But it is difficult to convince some of these people that the substance Laetrile is ineffective as a therapy for cancer when they have watched a film, listened to tapes, and heard testimonials from other patients, quite sincere in their beliefs that Laetrile has helped them" (*id.* at 3). He asks: "(I)s it a fair choice if (the cancer patients) are being pressured by Laetrile proponents?" (*id.*).

The constant efforts of Laetrile proponents are emphasized by those dealing with cancer patients. See, e.g., statement of Helene Brown, Executive Director of Community Cancer Control, Los Angeles, "that far from exercising a free and informed choice patients are confronted with enormous pressures to use Laetrile instead of conventional forms of therapy and that representatives attesting to the worth of

Laetrile make untrue, misleading and unsubstantiated claims" (R 393 at 5).

The presentations of the Laetrile proponents are made, as discussed in more detail elsewhere, to patients and families deprived of their normal decisionmaking abilities. See statement of John J. Dawson, M. Div., Director, Patient and Family Support, Mountain States Tumor Institute: "Research conducted at the Mountain States Tumor Institute and elsewhere indicates that the emotional trauma of a cancer diagnosis severely impairs the patient's and families' ability to engage in rational decisionmaking processes" (R 421 at 1).

Other submissions reflect a similar conclusion, see the statement of Rev. Reed: "The ability of (cancer patients and their families) to protect themselves is often severely limited by the emotional situation in which they find themselves" (R 418). (See also R 414 at 4; R 433 at ¶ 14.)

The Commissioner thus concludes as follows:

(1) To the extent that any freedom has been surrendered by the passage of the legislation which bans from the marketplace drugs that have not been proven to be effective, that surrender was a rational decision which has resulted in the achievement of a greater freedom from the dangers to health and welfare represented by such drugs.

(2) The choice of Laetrile therapy, by persons under the severe stresses associated with discovery of cancer and in response to misinformation presented

persuasively by Laetrile's proponents, cannot be regarded as a choice which is free.

#### D. ALLEGATIONS OF BIAS

Several submissions charged that FDA is too biased against Laetrile to conduct a fair hearing. Aside from general allegations of bias (R 313; R 248; R 353; R 507, R 302; R 73, Att. at 43; Tr. at 444-45), these submissions fall into two general categories: (1) the administrative rulemaking proceeding should have been conducted by someone other than FDA (R 144; R 505; R 222; Tr. at 12, 29, 75, 444-45); and, (2) the drug approval process administered by FDA is wrong (R 235; R 258; R 144; R 509; Tr. Ex. 1).

It is difficult for an agency charged with bias to rebut such charges persuasively. Nonetheless, the Commissioner feels that a complete decision requires some rebuttal of charges that he regards as erroneous and misdirected. Insofar as comments suggesting that the proceedings should have been conducted by someone other than FDA, it should be noted that FDA was required by court order to assemble an administrative record and make appropriate determinations therefrom. The task could not have been delegated to anyone else, and, even had the agency been able to do so, it is not likely that any tribunal chosen by FDA would have satisfied those persons who are convinced that the agency is biased. The FDA is, of course, the agency designated by Congress to evaluate the safety and effectiveness of drugs and, as such, it is the agency with expertise in this area.

The comments charging that the requirements for drug approval administered by FDA are wrong contained statements to the effect that testimonial evidence should be accepted as adequate proof of safety and effectiveness or that the cost of a clinical trial is too great a burden for the proponents of Laetrile to bear. Laetrile proponents place particular emphasis on the cost factors, stating that because clinical trials are expensive, FDA somehow favors only large drug companies.

As has been discussed above, FDA is bound by the requirements of law regarding drug safety and effectiveness. Those requirements have been challenged in court before, by the very drug companies toward whom Laetrile proponents allege FDA has a positive, favorable bias. These "favored" groups did not prevail, and the safety and effectiveness provisions were upheld.

*In Pharmaceutical Manufacturers Ass'n v. Richardson, supra*, a trade association whose membership includes major drug firms sought to enjoin the FDA regulations establishing the standards of evidence necessary to demonstrate the effectiveness of drug products (21 CFR 314.111). Pointing out that Congress could not have had testimonial evidence, clinical impressions, practical experience, or the unsubstantiated subjective views of medical practitioners in mind when it defined "substantial evidence," the court upheld the regulations. As one witness in the case pointed out, the approach which assumed that a collection of impressions would furnish the truth,

"did not prevent doctors from having unbounded faith in the curative powers of leeches for hundreds of years before scientific evaluation became the preferred means of judging efficacy of therapy" (318 F. Supp. at 307).

In *Upjohn Company v. Finch*, 422 F.2d 944 (6th Cir. 1970), a drug manufacturer sought review of an FDA order revoking marketing approval for seven combination antibiotic drugs. Stating that testimonial evidence was not enough to meet the standard of substantial evidence, the court held that "the record of commercial success of the drugs in question and their widespread acceptance by the medical profession, do not, standing alone, meet the standards of substantial evidence, prescribed by 21 U.S.C. 355(d)" (422 F. 2d at 954). Although the cost of developing the proper scientific evidence of safety and effectiveness is high, placing this burden upon those who wish to sell drugs is more than justified by the need to protect the consumer from harmful, useless, and fraudulent drugs.

The Commissioner acknowledges that the FDA is biased in one sense; the agency is committed to requiring that drugs meet the standards of safety and effectiveness required by law. The standards are designed to protect the public from drugs which are not both safe and effective. While the standards are rigorous, they are not mysterious. They are accepted by the scientific community and can be applied by any scientists who seriously wants to prove the value of a drug. The proponents of Laetrile choose to at-

tack the standards. They have not attempted to meet them.

#### E. LIMITING USE TO TERMINAL PATIENTS

There has been concern expressed in the submissions to the record that Laetrile might be approved for use by "terminal" cancer patients. Such an approval would be theoretically justified only on the grounds that since such patients might be considered beyond the help of other therapies, Laetrile cannot hurt them. Approval of a drug for use by terminal patients is not possible under the act; however, in light of the interest in this issue the Commissioner will discuss the evidence relating to it.

One submission objected to the possible use of Laetrile by terminal patients on the grounds that approval of such use constitutes sanction of an inhumane fraud upon the patients involved, one which wastes the financial resources of the patients and their families uselessly (R 190 at ¶ 17). Two other arguments were expressed by a number of submitters: (1) there is no such thing as a "terminal" patient and (2) allowing use by a subgroup of cancer patients would lead to increased use by patients who could be helped by legitimate therapy.

##### 1. Who is Terminal?

Dr. Peter H. Wiernik, Chief of the Clinical Oncology Branch of the National Cancer Institute's Baltimore Cancer Research Center, states, "One major



difficulty in making a particular chemical available for terminal patients only, is that no one can prospectively define the term 'terminal' with any accuracy. A patient can be said to be terminal only after he dies. Many patients who are critically ill respond to modern day management of cancer" (R 200 at ¶ 18).

D. Joseph F. Ross, Professor of Medicine at the University of California School of Medicine at Los Angeles, is actively involved in the medical care of cancer patients. He states, "[T]he distinction of 'terminal' patients from 'non-terminal' patients may not be reliably determined and an assumption that Laetrile may be given to such patients with impunity may deprive such patients of therapeutic measures which could help them" (R 190 at ¶ 17). Cf. R 393, Ex. 1 at 2: "Medical history is full of miracles." "No one knows if and when any patient is going to die." (Helene Brown, Executive Director of Cancer Control/Los Angeles); see also R 173, Att. "Questions Most Frequently Asked \* \* \*" at 2).

## 2. *Effects on Other Patients*

Approval for use of Laetrile by "terminal" patients, assuming some way could be found to define that class of individuals so as to exclude all those who might be helped by legitimate therapy, would still pose a risk to other patients who could be helped. This effect would, the evidence in the record shows, occur in two ways. First, approval for even this limited use would encourage illegitimate use of the type now occurring in this country.

Historian James Harvey Young, based upon his study of past "unproven" medical cures, states, "Permitting Laetrile's use in terminal cases gives it a credence among the public at large that will expand its use in early cases, for people will prefer taking a 'vitamin' to confronting the surgeon's knife" (R 400 at 11).

Dr. Samuel C. Klagsbrun, a psychiatrist who works with cancer patients at St. Luke's Hospital in New York, states, "Permitting Laetrile to be used by any population of cancer victims would have the correlative effect of creating the misimpression in the minds of other cancer victims that the drug is, in fact, safe and effective for a broader population" (R 433 at ¶ 12).

A second danger from such a limited approval of Laetrile is that the limitation would be extremely difficult to enforce. Kenneth A. Durrin, Acting Director, Office of Compliance and Regulatory Affairs, Drug Enforcement Administration, submitted an affidavit describing the detailed and costly regulation of "controlled substances" under the Controlled Substances Act (CSA) and then considered the possibility of approval of Laetrile "for terminal patients only" (R 435). He stated his conclusion as to the practicality of preventing the diversion of Laetrile from "terminal" patients, if approved for such patients, to others who might be helped by legitimate therapy: "Absent the kinds of controls available under the CSA—and indeed even with such controls—it is my opinion that a drug such as Laetrile could not effectively be restricted to a class of terminally

ill cancer patients. For example, absent a quota on production, manufacturers would not be limited to producing an amount of Laetrile sufficient only to provide a source of supply for terminally ill cancer patients. Manufacturers would not be restricted in the channels in which they could permissibly distribute the drug. They would not be required to report transactions in Laetrile. The amount of Laetrile which could be imported into this country would be unlimited.

"Given such unrestricted and unfettered availability of Laetrile, it is my opinion that there would be no practical way of limiting access to the drug to terminally ill cancer patients only. It is completely unrealistic to suggest that any other result would occur" (id. at ¶ 18-19).

The Commissioner concludes that approval of Laetrile restricted to "terminal" patients would lead to needless deaths and suffering among (1) patients characterized as "terminal" who could actually be helped by legitimate therapy and (2) patients clearly susceptible to the benefits of legitimate therapy who would be misled as to Laetrile's utility by the limited approval program or who would be able to obtain the drug through the inevitable leakage in any system set up to administer such a program.

#### F. USE CONCURRENTLY WITH OTHER THERAPY

Some persons not familiar with the problem of drug interactions have suggested that Laetrile might

be approved for use concurrently with legitimate cancer therapy. This theory would logically extend to allow any worthless drug to be used as long as effective therapy was also utilized. Such a limited use program would, of course, involve the problems of administration discussed in the previous section. Particularly in light of the Laetrile proponents' practice of disuading patients from what they characterize as the "cut, burn, and poison" techniques of legitimate therapy, any seeming government sanction of Laetrile would inevitably involve encouragement of use of "painless" Laetrile therapy alone and thus would result in needless suffering and loss of life (cf. R 191 at ¶ 17).

More important, it simply has not been shown by any sound scientific evidence that the administration of Laetrile along with other therapy may not either make such therapy more dangerous or interfere with its effects. Dr. James F. Holland states (R 396 at 2). "That Laetrile is inert as an anticancer drug does not mean it may not interfere with the metabolism of and compromise the effects from known anticancer treatments. This would require years of study to elucidate, and it is not a worthwhile undertaking since Laetrile itself has no anticancer activity. One does not seek further information on why not to use Laetrile. If there is no good reason to do something, the best reason exists not to do it" (emphasis in original). Thus, the same reasons that justify the law's ban on use of drugs not shown to be effective

form an equally strong basis for the ban on that use where the use will be concurrent with other therapy.

## VI. CONCLUSIONS

The Commissioner, after careful review of the administrative record amassed in this rule making proceeding, makes the following conclusions:

(1) Although the terms "Laetrile," "laetrile," "amygdalin," "Sarcarcinase," "vitamin B-17," and "nitriloside" have been used interchangeably, the chemical identity of the substances to which these terms refer has varied over the years. The identity of material referred to or called by any of those names is often not known. All too frequently terms have been used haphazardly or imprecisely by proponents, as well as opponents, of Laetrile:

"Laetrile," as described by Ernst T. Krebs, Jr., is: 1-mandelonitrile-*beta*-glucuronic acid.

"Amygdalin" is: D-mandelonitrile-*beta*-D-glucosido-6-*beta*-D-glucoside.

"Sarcarcinase" is the name given by Dr. E. T. Krebs, Sr., to a mixture of 6, possibly more, enzymes extracted from apricot pits.

(2) Neither Laetrile nor any other drug called by the various terms mentioned above nor any other product which might be characterized as a "nitriloside" is generally recognized by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs to be safe and effective for any therapeutic use.

(3) Animal studies conducted to date show that Laetrile has no anticancer activity in laboratory animals. Even if such activity were shown, the data would not be relevant to the issue of whether Laetrile is generally recognized by qualified experts as a safe and effective anticancer drug in humans.

(4) Neither Laetrile, amygdalin, nor any other drug called by the various terms set out in conclusion (1) is exempted from the "new drug" definitions of the act (21 U.S.C. 321(p)) by virtue of compliance with either the "1938 grandfather clause" (21 U.S.C. 321(p)(1)) or the "1962 grandfather clause" (section 107(c)(4) of Pub. L. 87-781).

(5) The history and promotion of Laetrile are characteristic of other unproven cancer remedies. Laetrile's popular acceptance by laymen lies not in credible proof of its effectiveness, but rather in the fears of orthodox medical treatment and the false hope, fostered by Laetrile's proponents, that suffering and eventual death can be avoided through Laetrile.

(6) Laetrile is not in general use as cancer therapy anywhere in the world.

(7) There is no evidence that "Vitamin B-17" is generally recognized among experts in the field of nutrition or nutrition research as a vitamin. Even if there were such recognition, "Vitamin B-17" would still be subject to regulation as a drug under the Federal Food, Drug, and Cosmetic Act because of the claims made for its use in cancer therapy.

(8) The safety of ingesting amygdalin, Laetrile and/or apricot or peach kernels or pits has not been



established. There is, in fact, evidence of frank toxicity from ingestion of the kernels or pits.

(9) There is no basis in law or in fact for the use of Laetrile or related substances in the treatment of cancer.

The foregoing opinion in its entirety constitutes the Commissioner's findings of facts and conclusion of law. Distribution of Laetrile, amygdalin, or any other substance called by the various terms set out in conclusion (1) in interstate commerce is in violation of the Federal Food, Drug, and Cosmetic Act and subject to regulatory action.

Dated: July 29, 1977.

DONALD KENNEDY,  
*Commissioner of Food and Drugs.*

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OCT 16 1978

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IN THE  
**Supreme Court of the United States**

OCTOBER TERM, 1978

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No. 78-605

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UNITED STATES OF AMERICA, *et al.*,  
*Petitioners*

v.

GLEN L. RUTHERFORD, *et al.*,  
*Respondents*

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On Petition for a Writ of Certiorari to the United States  
Court of Appeals for the Tenth Circuit

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**MOTION FOR LEAVE TO FILE BRIEF AMICUS CURIAE  
AND BRIEF AMICUS CURIAE OF THE AMERICAN  
CANCER SOCIETY IN SUPPORT OF THE  
PETITION FOR CERTIORARI**

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**MOTION FOR LEAVE TO FILE BRIEF AMICUS CURIAE**

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The American Cancer Society ("Society") respectfully requests leave to file *instantly* the within brief *amicus curiae* in support of the United States' petition for writ of certiorari. The interest of the Society and its participation in the "Rulemaking Proceedings On Laetrile" before the Food and Drug Administration ("FDA") (Petitioners' Appendix at 51a) and as *amicus curiae* without opposition in the proceedings on appeal in the United States Court of Appeals for the Tenth Circuit (Petitioners' Appendix at 10a), is as stated in the "Statement of Interest" in the attached brief.



By letter of October 10, 1978, the Solicitor General of the United States, Wade H. McCree, Jr., consented "to the filing of a brief *amicus curiae* on behalf of the American Cancer Society in the Supreme Court in this case."

By letter of October 6, 1978, the undersigned counsel for the Society contacted Mr. Kenneth Coe, Esquire, attorney of record for the *Rutherford* plaintiffs below, requesting the same consent. This letter was followed up by a phone call on the afternoon of October 11, 1978. Mr. Coe flatly refused to grant consent. In so doing he cited as his reason, the lack of cooperation and run-around which he had received from the FDA in the prior proceedings which, of course, have no bearing on the propriety of an *amicus* brief to the Supreme Court by the Society.

While the Society supports the position of the Petitioner, the United States, its brief presents a different perspective, one which is in keeping with the role of the Society.

The Society is a voluntary organization fighting cancer through balanced programs of research, education, patient service and rehabilitation. The American public and the medical profession look to the Society for the most up-to-date and accurate information about cancer. Without the widespread dissemination of accurate information, such as that provided by the Society, the goal of further reducing the ravages of cancer through early diagnosis and treatment would unquestionably be more difficult to achieve.

Inasmuch as early and proper treatment of cancer is a life-and-death matter, unjustified deviations from this desideratum are of concern to the Society. One of the areas in the forefront of public and professional questioning addressed to the Society pertains to unproven methods of cancer management, e.g., laetrile.

It is from this perspective that the Society approaches participation as an *amicus curiae* in this proceeding. The Society's brief is not a repetition of arguments made by the United States or, we anticipate, by the respondent, but rather deals with and contains matter related to the impact of the Court of Appeals decision excluding the terminally ill from the coverage of the federal drug laws, both on the terminally ill as well as on those with life-threatening illness. The Society's brief deals with the issues of the role of the federal government with respect to the regulation of drugs in a manner and from a viewpoint different from that of the other parties.

The Society believes, in view of the nature of the case at bar, and the arguments urged or anticipated from the parties, that its arguments and information will assist the Court in its decision on the petition and that the Society should therefore be granted leave to file its brief *amicus curiae* in support of the Government.

Respectfully submitted,

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October 16, 1978

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IN THE  
**Supreme Court of the United States**

OCTOBER TERM, 1978

\_\_\_\_\_  
 No. 78-605  
 \_\_\_\_\_

UNITED STATES OF AMERICA, *et al.*,  
*Petitioners*

v.

GLEN L. RUTHERFORD, *et al.*,  
*Respondents*

\_\_\_\_\_  
 On Petition for Writ of Certiorari to the United States  
 Court of Appeals for the Tenth Circuit  
 \_\_\_\_\_

BRIEF AMICUS CURIAE OF THE AMERICAN CANCER  
 SOCIETY IN SUPPORT OF THE PETITION  
 FOR CERTIORARI

\_\_\_\_\_  
 STATEMENT OF INTEREST OF THE  
 AMERICAN CANCER SOCIETY

The American Cancer Society has a substantial interest in the outcome of this proceeding. Briefly stated, the American public and the medical profession look to the American Cancer Society to provide the most up-to-date and accurate information about cancer. Since early and effective treatment of cancer is a life and death matter, one of the areas in the forefront of the public and pro-

fessional questioning addressed to the Society pertains to unproven methods of cancer treatment. In its efforts to respond to the need for information in this area, the Society established a committee on unproven methods and maintains the world's largest reference center for the collection and dissemination of data concerning the subject. In furtherance of its obligation to the American public and the medical profession to uncover and disseminate the facts relating to unproven methods of cancer treatment, the Society participated in the Food and Drug Administration rulemaking proceeding which followed the legal parameters set by the Court of Appeals in *Rutherford v. United States*, 542 F.2d 1137, 1140-43 (10th Cir. 1974). (Petitioners' Appendix at 51d). The Society also participated as *amicus curiae* in the proceedings on appeal which are the subject of this petition for writ of certiorari (Petitioners' Appendix at 10a).

The outcome of the Government's petition for certiorari which the Society supports will be largely determinative of whether the protections provided by Congress to the American public in the Food, Drug and Cosmetic Act will survive or whether they will fall, depriving both the consumer and the practicing physician of the first line of defense established by Congress at the request of President Kennedy who stated:

There is no way of measuring the needless suffering, the money innocently squandered, and the protraction of illnesses resulting from the use of . . . ineffective drugs.

The physician and consumer should have the assurance from an impartial scientific source, that any drug or therapeutic device on the market today is safe and effective for its intended use . . . .

1962 U.S. Code Cong. & Admins. News at 4143-44. The impact of the *Rutherford* Court of Appeals decision on the federal drug standards of safety and efficacy will

obviously affect the Society in its role as primary information source to the general public and the medical profession for accurate information on unproven methods of cancer treatment.

Another indication of the impact of the *Rutherford* decision, should it stand, on the public, and on the Society as its information resource, lies in the resurgence since mid-1976 when the *Rutherford* suit became heavily publicized, of inquiries about a number of unproven methods of cancer treatment in addition to laetrile. Prior to the *Rutherford* publicity, some of these methods were quiescent for months or years or came to the Society's attention at long scattered intervals. Those unproven methods include, e.g., the biological theory of ironization; herbal remedies including one called essiac; chelation therapy and alleged vaccines combined with special diets.

If the Court of Appeals' decision is permitted to stand, it will open the floodgates and permit the public, particularly those with life-threatening illness who are choice prey, to be inundated by worthless and therefore unsafe and dangerous drugs. The Society's interest lies in speaking out for the continuation of the proper balance of manufacturer and consumer interests which currently exists in the statutory scheme relating to drugs. It would be a grave disservice to the public if this regulatory scheme were undermined on the basis of a Court of Appeals decision which we demonstrate below is unsound as a matter of law.

## REASONS FOR GRANTING THE WRIT

### I. THE COURT OF APPEALS BY REWRITING THE FEDERAL DRUG LAWS HAS SO FAR DEPARTED FROM THE ACCEPTED AND USUAL COURSE OF JUDICIAL PROCEEDING AS TO CALL FOR AN EXERCISE OF THIS COURT'S POWER OF SUPERVISION

#### A. From The Exercise Of Federal Authority Over Drugs Initially By The Act Of 1906, And As Amended, The Terminally Ill Lay Within The Special Protection Of The Acts

The medical and popular press in the early 1900's reflected the sense of the country at that time that the words cancer and terminal illness were interchangeable. E. Cuyler Hammond, D.Sc., Director of Statistical Research Section of the American Cancer Society, writing in 3 *Cancer* 417 (Butterworth & Co., London, 1958) described the public's impression of cancer in the first quarter of this century as "incurable" and further stated that this conception was shared by a large proportion of the medical profession. This impression was certainly borne out by the literature which reported the survival rate for, e.g., uterine cancer in 1900, to be as low as 2.8%.<sup>1</sup>

Although these statistics improved somewhat in that between 1935-1940, the five year survival rate for all sites of cancer combined had reached 25% and by

<sup>1</sup> T. S. Cullen, *Cancer of the Uterus* (1900). See also, E. C. Hammond, "Cancer Prevention of Comparative Risks", 19 *Archives of Environmental Health* 395 (1969); and see J. S. Bloodgood, "Responsibility of the Medical Profession for Cancer Education, with Special Reference to Cancer of the Cervix", 15 *American Journal of Cancer* 1579 (1931) ("cancer of the cervix is today predominantly a hopeless disease.").

1951 it had reached 32%,<sup>2</sup> even in 1967, public and physician reaction to the term cancer still equated it with a death sentence:

Cancer has many unconscious meanings and fantasies associated with it. Whatever the unconscious feelings which it stirs, typically it is feared consciously as a process equated with suffering and certain death . . . People continue to think of cancer as 'the killer.'

What is impressive is that the doctors themselves feel very much the same way. It was not patients who described the diagnosis as a 'death warrant' or 'a date of execution.' The internist who referred to cancer as an 'incurable disease with an inevitable demise' expressed a view which was not atypical.<sup>3</sup>

As late as the summer of 1977, in Hearings before Senator Edward Kennedy's Subcommittee on Health and Scientific Research,<sup>4</sup> Lewis Thomas, M.D., Director of the Memorial Sloan-Kettering Cancer Center, observed that "For many patients and their families, the very word cancer is perceived as a death sentence. It is widely believed to be an inexorable and agonizing process, with no way out but death."<sup>5</sup>

<sup>2</sup> E. C. Hammond, "The Possibility of Improving Cancer Cure Rates at the Present Time", *Cancer*, May-June 1957 at 581-82; *Proceedings of the Third National Cancer Conference* 910 (1957).

<sup>3</sup> Donald Oken, "What to Tell Cancer Patients: A Study of Medical Attitudes", reprinted in Weir, *Ethical Issues in Death and Dying* (1977) at 21.

<sup>4</sup> Hearings Before the Subcommittee on Health and Scientific Research of the Senate Committee on Human Resources, "Evaluation of Information on Which the FDA Based Its Decision To Ban The Drug Laetrile From Interstate Commerce", 95th Cong., 1st Sess. ["Laetrile Hearings"].

<sup>5</sup> Laetrile Hearings, *supra* at 13.

This "popular" belief contrasts strongly with the actual statistics relating to survival from cancer which show that today, due to earlier diagnosis and the steady improvement in surgical, x-ray and



The early concern of the public and the press that the "seriously" or "terminally" ill be protected from useless nostrums is perhaps best exemplified by a series of articles by Samuel Hopkins Adams published in Collier's Weekly in 1906. These articles sought to enlighten the general public regarding the effects of various patent medicines and provided substantial impetus for the 1906 legislation regulating drugs.<sup>6</sup> A segment of the series contained the following passage, entitled "Preying on the Incurables":

Incurable disease is one of the strongholds of the patent-medicine business. The ideal patron, viewed in the light of profitable business, is the victim of some slow and wasting ailment in which recurrent hope inspires to repeated experiments with any "cure" that offers. In the columns of almost every newspaper you may find promises to cure consumption. Consumption is a disease absolutely incurable by any medicine . . . This is thoroughly and definitely understood by all medical and scientific men. Nevertheless there are in the patent-medicine world a set of harpies who, for their own business interests, deliberately foster in the mind of the unfortunate sufferer from tuberculosis the belief that he can be saved by the use of some absolutely fraudulent nostrum. Many of these consumption cures contain drugs which hasten the progress of the disease . . . Others are comparatively harmless in themselves, but by their fervent promises of rescue they delude the sufferer into misplacing his reliance and forfeiting

chemical approaches to the management of cancer, the ratio of patients alive after five years of disease is one in three. With even earlier diagnosis and prompt treatment, half of those who have cancer could be saved. See American Cancer Society, 1977 Cancer Facts and Figures.

<sup>6</sup> See Cramp, Nostrums & Quackery (1912) for a compilation of the Colliers articles and a discussion of their effect on the food and drug legislation of 1906.

his only chance by neglecting those rigidly careful habits of life which alone can conquer the "white plague." One and all, the men who advertise medicines to cure consumption deliberately traffic in human life.<sup>7</sup>

The inclusion of several of the Collier's Articles in the Congressional Record<sup>8</sup> as well as numerous citations in the Pure Food and Drug Act debates of reported frauds perpetrated upon the victims of such serious illness as cancer, consumption and diabetes in the form of spurious claims for cures,<sup>9</sup> indicates a significant concern with those illnesses which in 1906 were "terminal" and by inference a determination by Congress that the "terminally ill" as a class would be protected by the legislation.

Given this background of concern over the coverage of the 1906 Act vis a vis cancer, consumption and other illness then considered fatal, the Congress expressed disbelief when the Supreme Court in *United States v. Johnson*, 221 U.S. 288 (1911), a case which concerned a purported treatment for cancer, over a strong dissent by Justice Hughes, held that the 1906 Act did not apply to misrepresentations of facts relating to the ability of a drug to treat or cure a disease, but rather, only as to whether the ingredients used in the drug were properly stated on the label.

In response to this opinion, President Taft, on June 21, 1911, in a message to Congress, urged action to protect the seriously ill against statements of curative effect on drugs that are contrary to fact and that seduce the ill away from proven medical treatments:

An evil which menaces the general health of the people strikes at the life of the Nation. In my opin-

<sup>7</sup> 48 Cong. Rec., part 12, Appendix at 625-630.

<sup>8</sup> *Id.*

<sup>9</sup> See e.g., 40 Cong. Rec. 1416, 9073.

ion, the sale of dangerously adulterated drugs, or the sale of drugs under knowing false claims as to their effect on disease, constitutes such an evil and warrants me in calling the matter to the attention of the Congress.

Fraudulent misrepresentations of the curative value of nostrums not only operate to defraud purchasers but are a distinct menace to the public health. There are none so credulous as sufferers from disease. The need is urgent for legislation which will prevent the raising of false hopes of speedy cures of serious ailments by misstatements of facts as to worthless mixtures on which the sick will rely while their diseases progress unchecked.<sup>10</sup>

The Congress reacted to this call for action by passing the Sherley Amendment to the Act [Act of August 23, 1912, 37 Stat. 416, ch. 352] which provided that misstatements regarding curative or therapeutic effects of a drug or device fall within the ambit of the Act.

In commenting upon the Sherley Amendments to the Act in the 1913 Report of the Bureau of Chemistry, Bureau Chief Carl L. Alsberg notes the early successes of the Amendment in terms of the curative claims found on medicinal labels. According to Alsberg, "Claims that preparations are cures for such serious diseases as tuberculosis or cancer do not appear on the labels as often as formerly."<sup>11</sup>

The reach of the protection of the statute to those who suffer from untreatable or incurable disease is apparent from the opinion of Justice Hughes upholding the Sherley Act Amendment to the 1906 Act in *Seven Cases . . . Eckman's Alternative et al. v. United States*, 239 U.S.

<sup>10</sup> 48 Cong. Rec. 11322 (1911). See also, *Belmont Laboratories v. FTC*, 103 F.2d 538 (3d Cir. 1939).

<sup>11</sup> Federal Food and Cosmetic Law, Administrative Reports, 1907-1949, CCH, Food Law Institute Series (1951).

510, 514 (1916). Justice Hughes, speaking for the Court, specifically upheld the following libel as a matter subject to prosecution under the Act as amended:

[The label] conveys the impression to purchasers that said article or drugs will cure tuberculosis, or consumption, whereas, in truth and in fact, said article of drugs would not cure tuberculosis, or consumption, *there being no medicinal substances known at present which can be relied upon for the effective treatment or cure of tuberculosis, or consumption.* (emphasis added).

The concern of Congress that the protection of the Food, Drug and Cosmetic Act be extended not just to "healthy" consumers or those with life-threatening illness, but also to those with a terminal or fatal illness is also present in the Congressional debate on the 1962 amendments to the Act—which added the effectiveness requirement for new drugs.<sup>12</sup> Language in the debates reflects an understanding that the Act would apply to experimental drugs used to treat "cancer in its last stages."<sup>13</sup> Senator Eastland, another proponent of the bill, also assumed that drugs administered for "fatal diseases, such as cancer," would be subject to the Act's requirements, noting that approval of such drugs would be appropriate even though they might only prolong life or alleviate suffering.<sup>14</sup>

In view of this Court's interpretation of the amendments to the 1906 Act as progressively strengthening and

<sup>12</sup> See *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609 (1973). With respect to the concern regarding cancer demonstrated in the debates on the 1938 amendments to the Act, see e.g., 79 Cong. Rec. 5023 (1935) (remarks of Sen. Copeland); 83 Cong. Rec. 7786-89 (1938) (remarks of Rep. Phillips and Rep. Lea).

<sup>13</sup> 108 Cong. Rec. 17399 (1962) (remarks of Sen. Kefauver, Chairman of the committee reporting the bill).

<sup>14</sup> 108 Cong. Rec. 17401 (1962) (remarks of Sen. Eastland).

extending that law's protection of the consumer,<sup>15</sup> and the continuing evidence of concern by Congress with diseases that were considered "fatal", the protection afforded terminally ill patients under the Act has even greater force and effect today.

The plain language of the Act,<sup>16</sup> its legislative history set forth above, the holding of this Court that the Act is to be given a liberal construction<sup>17</sup> and should not be narrowed in coverage "short of the point where Congress indicated it should extend",<sup>18</sup> all point out the error inherent in the Court of Appeals' decision which carved out an exception from the Act for terminally ill patients. The Court has usurped the role of the Congress by re-writing the Act. The departure of the Court of Appeals from the role of the judiciary parallels a similar departure noted by this Court in *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969). The petition for certiorari was granted in that proceeding to permit correction of that error; that same course of action is indicated here:

The historical expansion of the definition of drug, and the creation of a parallel concept of devices,

<sup>15</sup> See e.g., *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 793-99 (1969); *United States v. Dotterweich*, 320 U.S. 277, 280-82 (1943); *United States v. Sullivan*, 332 U.S. 689, 697 (1938).

<sup>16</sup> Section 201(f) of the Food, Drug and Cosmetic Act provides in part:

The term "new drug" means—(1) Any drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof. . . .

<sup>17</sup> *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. at 798. And see *United States v. Lee*, 131 F.2d 464 (7th Cir. 1942).

<sup>18</sup> 394 U.S. at 801.

clearly show, we think, that Congress fully intended that the Act's coverage be as broad as its literal language indicates—and equally clearly, broader than any strict medical definition might otherwise allow. Strong indications from legislative history that Congress intended the broad coverage the District Court thought "ridiculous" should satisfy us that the lower courts erred in refusing to apply the Act's language as written. But we are all the more convinced that we must give effect to congressional intent in view of the well-accepted principle that remedial legislation such as the Food, Drug, and Cosmetic Act is to be given a liberal construction consistent with the Act's overriding purpose to protect the public health, and specifically, § 507's purpose to ensure that antibiotic products marketed serve the public with "efficacy" and "safety." Cf. *United States v. Sullivan*, 332 US 689, 693-695, 92 L Ed 297, 301, 302, 68 S Ct 331 (1948); *United States v. Dotterweich*, 320 US 277, 283-284, 88 L Ed 48, 52-53, 64 S Ct 134 (1943).

394 U.S. 798.

## II. THE COURT OF APPEALS DECISION CARVING OUT AN EXCEPTION FROM THE COVERAGE OF THE FEDERAL DRUG LAWS FOR THE TERMINALLY ILL IS IN CONFLICT WITH THE DECISIONS OF OTHER COURTS OF APPEAL

The Court of Appeals' conclusion "as a matter of law that the 'safety' and 'effectiveness' terms used in the statute have no reasonable application to terminally ill cancer patients, and have no established meaning when considered in that context"<sup>19</sup> is in conflict with *Rutherford v. American Medical Association*, 379 F.2d 641 (7th

<sup>19</sup> Petitioners Appendix at 3a.



Cir. 1967), *cert. denied*, 389 U.S. 1043<sup>20</sup> and also with *Tutoki v. Celebrezze*, 375 F.2d 105 (7th Cir. 1967).<sup>21</sup>

The *Allen Rutherford* case involved an action for a permanent injunction against the FDA and others by a physician and a number of cancer patients requiring that agency and others to cease their interference with the distribution, for their use, of the alleged cancer drug Krebiozen. Krebiozen had not received new drug approval from the FDA and hence was unavailable in interstate commerce. The Court of Appeals "sympathetically viewed" the action as "an outcry of *hopeless*, suffering cancer victims." 379 F.2d at 642. However, the Court did not reach the conclusion that the Act does not apply to such "*hopeless*" cancer victims, but rather, in denying their claim for injunctive relief, held that the right to such relief must be accompanied by a showing that under the procedures established by Congress for the introduction of new drugs, the drug Krebiozen would be approved or exempted (grandfather clause application) by the FDA.

In the *Tutoki* case, the Court of Appeals was asked to issue a declaratory judgment that the approval and exemption provisions of the federal laws relating to food and drugs do not apply to cancer patients and the drug they seek,—Krebiozen. 375 F.2d at 106. The *Tutoki* Court, specifically faced with the issue whether the federal drug laws were appropriately applied to cancer patients, mirrored the conclusions of the *Allen Rutherford* court,—that the FDA procedures cannot be bypassed unless it can be shown that the FDA, if it acted upon Krebiozen, would have approved or exempted the drug.

<sup>20</sup> Hereinafter referred to as the "*Allen Rutherford*" case to distinguish it from the *Glen Rutherford* case which is the subject of this petition for writ of certiorari.

<sup>21</sup> Hereinafter referred to as "*Tutoki*".

The *Allen Rutherford* and *Tutoki* opinions thus postulate the provisions of the drug laws as applying to "*hopeless*" cancer patients,—the exact opposite of the result urged by the *Glen Rutherford* Court of Appeals.<sup>22</sup> A conflict between circuits is present requiring the resolution of this Court.

### III. THE COURT OF APPEALS HAS DECIDED AN IMPORTANT QUESTION OF FEDERAL LAW, NAMELY, WHETHER THE TERMINALLY ILL SHOULD BE EXCLUDED FROM THE COVERAGE OF THE FEDERAL DRUG LAWS, WHICH HAS NOT BEEN, BUT SHOULD BE SETTLED BY THIS COURT

#### A. Terminal Cancer Patients Require the Protection of the Act

The Court of Appeals in the *Rutherford* case poses the question:

[W]hat can "generally recognized" as "safe" and "effective" mean to such persons who are so fatally stricken with a disease for which there is no known cure? <sup>23</sup> What meaning can "effective" have in the absence of anything which may be used as a standard. Under this record Laetrile is as effective as

<sup>22</sup> Cf. *United States v. Olsen*, 161 F.2d 669 (9th Cir. 1947) in which the requirements of the federal laws relating to drugs were considered applicable to a patient/purchaser of a device advertised as diagnosing, mitigating, treating, preventing or curing a variety of ailments.

<sup>23</sup> This finding flies in the face of administrative and court interpretation which has hitherto consistently found the Act and its safety and effectiveness provisions applicable to cancer patients. See e.g., Hearings on S. 1552 Before the Subcomm. on Antitrust and Monopoly of the Senate Comm. on the Judiciary 87th Cong., 1st Sess. Part 5, at 2588 at which the Secretary of HEW explained the FDA's attitude as follows: "If the drug is offered for the treatment of progressive or life threatening diseases *such as cancer*, or if the drug is seriously toxic or has alarming side effects we now consider its effectiveness." (emphasis added). See also, *Durovic v. Richardson*, 479 F.2d 242 (7th Cir. 1973), *cert. denied*, 414 U.S. 944.

anything else. What can "effective" mean if the person, by all prevailing standards, and under the position the Commission takes, is going to die of cancer regardless of what may be done. (Petitioners Appendix at 6a).<sup>24</sup>

The Court of Appeal's focus is apparently restricted to "cure" and is thus too narrow in terms of the class it addresses,—the terminally ill.<sup>25</sup> Bernard C. Meyer in an article "Truth and the Physician" reprinted in *Ethical Issues in Death and Dying* (1977) at 53, observes that the "Physician's response once he can no longer arrest disease is to assuage discomfort and distress". A cure may not be possible, but other relief for the terminally ill may be, for example, pain control, appetite stimulation, tranquilization.

In the Laetrile Hearings it became clear that the purveyors of laetrile have moderated their claims for the substance in recent years. For the most part, it is no longer openly claimed<sup>26</sup> that laetrile cures cancer [al-

<sup>24</sup> There is inconsistency in the Court of Appeals finding that the terminally ill are excluded from the strictures of the Act while at the same time confining the utilization of laetrile to an injection route.

<sup>25</sup> For the purposes of this petition, it is assumed that an objective standard to determine who is "terminally ill" can be formulated and applied. However, applicability of the term terminal to individual patients is fraught with uncertainty in the context of cancer patients and if the petition is granted, the unworkability of the exclusion of this class from the statute will be fully explored.

<sup>26</sup> Compare the remarks of Lewis Thomas, M.D., Director of the Memorial Sloan-Kettering Cancer Center at Laetrile Hearings pp. 13-14 ("It is no longer openly claimed that Laetrile cures cancer", although some of the leaflets and public releases hint broadly in this direction.") with the remarks of Senator Kennedy at p. 257: "... the thing that's interesting about your careful choice of words about the impact of this [Laetrile] would be you had no reluctance of using the word 'cures' or 'recoveries' in the transcripts here before the California case. It was a tape of the town meeting. And I'll just read: 'Some cases have undergone clinical arrests, or for other practical purposes, we might describe as cures or recoveries.'"

though this is the expectation of the cancer victims that turn to it]. The current thrust of the laetrile proponents seems to be that it will dramatically relieve pain, improve appetite, promote weight gain, reduce the odor associated with cancer, improve the cancer patients general sense of well-being, control or prevent cancer.<sup>27</sup>

The terminally ill are entitled under the Act to the assurance that the products they seek to use are effective not only for cure or treatment but also for these other purposes.

Cancer victims constitute a minority group in our society; terminal cancer patients constitute an even smaller minority, but like other groups, they have a right not to be exploited. In the case of cancer drugs, particularly the exercise of government power of protection, pre-market clearance is not only reasonable, but necessary to protect the compelling public interest in effective cancer therapy, and in assuring that non-therapeutic drugs do what they say. In view of the widespread incidence of cancer, the serious consequences of the disease, the experience with the particular vulnerability of cancer patients and their families to promoters of easy money-making schemes labeled in mysterious scientific dress, it is imperative that the standards of consumer protection set forth in the federal drug acts be maintained.

<sup>27</sup> See e.g., Laetrile Hearings at pp. 13-14 (Dr. Thomas); J. A. Richardson, M.D. who prescribes laetrile at 246-247, 271-72 (prevention, control, pain relief, appetite increase, weight gain, feeling of well-being). Robert A. Bradford, Committee on Free Choice for Cancer Treatment at 295-297 (stimulation of appetite, weight gain, decrease or eliminate pain, bad odor, pallor). Mr. Bradford also stated at p. 295 that "Laetrile is not offered as a cancer cure. There is no cure for cancer . . . In the very best of instances it may effect a control—but not a cure—of cancer. . . .". See also the opinion of the Commissioner of the FDA at Petitioners Appendix pp. 73a-78a.

Further, the Court of Appeals assumes that Laetrile by injection is safe.<sup>28</sup> This assumption is unsupported by the record before the Court. An awareness of the actual and potential toxicity of Laetrile has emerged in recent expressions of scientific opinion.<sup>29</sup> Of particular significance is the article "Laetrile Toxicity: A Report of Two Cases", Smith and Schein, 238 *Journal of the American Medical Ass'n* 1361 (Sept. 1977). This article describes a case of serious side effects relating to administration of laetrile by injection and the cessation of such side effects when the laetrile was withdrawn.

<sup>28</sup> The Court of Appeals direction to the FDA to promulgate regulations relating to the use of laetrile by injection by the terminally ill, cannot be executed. The laetrile proponents have been unable to provide a consistent picture of what the components of laetrile is. The samples alleged to be laetrile seized and analyzed by the FDA have had differing chemical compositions. Specifically, Commissioner Kennedy testified at pp. 4-5 of the Laetrile Hearings that the substance "has no fixed identity in the literature of its own components. It also has no fixed identity in the hands of our analytical chemists who find that the amount of amygdalin and the ratio of its isometric forms varies widely in the samples of materials we had seized." See also the Commissioners Opinion at Petitioners Appendix at 182a-187a.

Compare, *Durovic v. Richardson*, 479 F.2d 242, 251 (7th Cir. 1973), *cert. denied*, 414 U.S. 944. In that case, the Court of Appeals, as one rationale for its decision that Krebiozen could not be generally recognized as safe even in the narrow sense of non-toxic by qualified experts found that as of "October 9, 1962, the identity and composition of Krebiozen was completely unknown."

<sup>29</sup> See e.g., Jukes, "Laetrile For Cancer," 236 *Journal of the American Medical Ass'n* 1284 (1976); Humbert, "Fatal Cyanide Poisoning: Accidental Ingestion of Amygdalin," 238 *Journal of the American Medical Ass'n* 482 (1977) and Lewis, "Laetrile" 127 *Western Journal of Medicine* 55 (1977).

## **B. Approval Of Laetrile For The Terminally Ill Poses A Substantial Threat To Those Whose Cancer Is Merely Life-Threatening**

Finally, approval of laetrile for the terminally ill would pose a substantial threat to those whose cancer was merely "life-threatening". This very real danger was noted by Dr. Lewis Thomas at the Laetrile Hearings at p. 14:

It is often asserted that since Laetrile is not a particularly toxic substance, it should be made available to all patients who wish to use it as a matter of free choice. There is, however, a very real danger here. If, for example, children with early leukemia or sarcoma, or women with cancer of the breast, or young men with Hodgkin's disease, are persuaded to give Laetrile a trial before doing anything else, the outcome will almost certainly be death, in circumstances where appropriate therapy could be lifesaving.

Further, approval of laetrile for the terminally ill would give the appearance of an official imprimatur, and would encourage use of the drug by patients who could be helped by legitimate therapy. See the Commissioner's Opinion at Petitioners' Appendix p. 268a. James Harvey Young, a noted medical historian, testified on the basis of his study of past unproven cures that "[p]ermitting laetrile's use in terminal cases gives it a credence among the public at large that will expand its use in early cases, for people will prefer taking a 'vitamin' to confronting the surgeon's knife." Petitioners' Appendix at 269a. Dr. Samuel G. Klagsbrun, a psychiatrist who works with cancer patients at St. Luke's Hospital in New York, testified that "[p]ermitting laetrile to be used by any population of cancer victims would have the correlative effect of creating the misimpression in the minds of other cancer victims that the drug is, in fact, safe and effective for a broader population." Petitioners' Appendix at 269a.



Also, laetrile cannot be effectively restricted to a "class" of "terminally ill" cancer patients. The experience in this country in regulating other controlled substances, available for limited use (e.g., cocaine), highlights the impossibility of restricting laetrile to "terminally ill" cancer patients, and preventing broader promotion. Petitioners' Appendix at 269a-270a.

The dangers posed by approval of laetrile for the terminally ill are particularly clear in the case of children with cancer. Children constitute only one percent of the cancer cases in this country but cancer represents the most serious threat to childlife next to accidents. Childhood cancers are also the category in which the greatest success in long-term remission and "cures" have been made. Yet, the natural desire for parents to avoid the suffering for their child which is a part of conventional treatment makes this class a minority which requires protection from the loophole in the law advanced in the *Rutherford* Court of Appeals decision.

This need is illustrated by a recent Massachusetts case arising from a physicians request to have a child committed to the Department of Public Welfare for the purpose of providing necessary medical care (chemotherapy) for the treatment of leukemia. *Custody of A Minor*, S.J.C. No. P-1422, Mass. Supreme Court, July 10, 1978 affirming the decision of the Superior Court, Plymouth Division of April 18, 1978 in Civil Action No. 78-6916.

#### IV. OTHER ISSUES INHERING IN THE CASE WHICH REQUIRE THAT THE PETITION FOR CERTIORARI BE GRANTED

Since the Court of Appeals has rewritten the Food, Drug and Cosmetic Act in ways which significantly endanger the public health and in particular the health

of those whose illness is life-threatening as distinguished from terminal, and since that decision conflicts with the decisions of other Courts of Appeals, the grounds set forth in Arguments I-III *supra* are sufficient to warrant the grant of the Government's petition for certiorari.

However, it is anticipated that the respondents may argue in reply to the petition that if the Court of Appeals cannot be sustained on its exclusion of the terminally ill from the statute, it should be upheld on the other grounds not dealt with by that Court, but contained in the District Court opinion. It is anticipated that the grounds alleged will be (1) that the substance Laetrile is protected by the grandfather clause in the 1962 Act, and that (2) the right to take laetrile is constitutionally protected. If these arguments are raised, the American Cancer Society would argue in its brief on the merits that (1) Laetrile is a new drug which is not exempt under the 1962 Grandfather Clause from the statutory premarketing clearance requirements of the Act; and (2) that the use of Laetrile is not constitutionally protected, specifically that Congress does not exceed its recognized authority to protect the public health and welfare in prohibiting the interstate movement of any drug which is not recognized as safe and effective.

#### CONCLUSION

Statutes should be given their fair meaning in accord with the evident intent of Congress. See e.g., *United States v. Sullivan*, 332 U.S. 689 (1948) and *United States v. Raynor*, 302 U.S. 540 (1938). The Court of Appeals has departed from this principle by construing the Act in a way that conflicts with its plain meaning and statutory intent, thereby eroding the protections provided by the Act and posing a significant threat, particularly to those whose illness is life-threatening instead of terminal.

For these reasons, the Government's petition for a writ of certiorari should be granted by this Court.

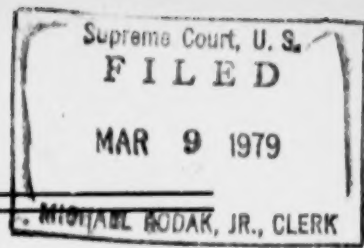
Respectfully submitted,

GRACE POWERS MONACO  
FAIRMAN, FRISK & MONACO  
Suite 301B  
2600 Virginia Avenue, N.W.  
Washington, D.C. 20037

Attorney for the  
American Cancer Society

October 16, 1978

APPENDIX



**In the Supreme Court of the United States**

OCTOBER TERM, 1978

No. 78-605

UNITED STATES OF AMERICA, ET AL.,  
*Petitioners*

—v.—

GLEN L. RUTHERFORD, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES  
COURT OF APPEALS FOR THE TENTH CIRCUIT

PETITION FOR WRIT OF CERTIORARI FILED OCTOBER 10, 1978  
CERTIORARI GRANTED JANUARY 22, 1979



**In the Supreme Court of the United States**

OCTOBER TERM, 1978

**No. 78-605**

UNITED STATES OF AMERICA, ET AL.,  
*Petitioners*

—v.—

GLEN L. RUTHERFORD, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES  
COURT OF APPEALS FOR THE TENTH CIRCUIT

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(1)

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CIV—75-021 8-B

Closed Dec. 5, 1977

RUTHERFORD, GLEN L., PLF INTERVENOR

and

STOWE, JIMMIE, and SCHNEIDER, GENE, individually and on behalf of a class composed of cancer victims and their spouses, who are responsible for the costs of treatment, ORIGINAL PLAINTIFFS

WARD, IRENE, INTV. 1-8-76

v.

UNITED STATES OF AMERICA and WEINBERGER, CASPER, Secretary of Health, Education and Welfare, DEFENDANTS

DATE INTERVENERS

---

1-26-76	Ruth O. Aldrich
4-23-76	LaVerne Martin
4-23-76	Helen W. Wallace
4-23-76	Hazel Ward Ahrens
5-24-76	Charles Eugtne Gassaway
6-3-76	Barbara C. Hopping
6-10-76	David M. Davis
6-23-76	Tom Covington
11-26-75	Ernest Ray
6-24-76	Donna Vivian Auer
7-9-76	Phillip C. Ferguson
7-9-76	Myrtle M. McCluskey
7-9-76	Helen Hook
7-15-76	Edna May Ingram
8-4-76	Juanita Loftiss
8-4-76	Mary Ferris
8-12-76	Helen B. Wilson
9-22-76	Muriel R. McWilliams
9-22-76	Orian T. Carroll
10-6-76	Sidney Elmer White
10-6-76	Corie Lynn Mudd

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DATE      INTERVENERS

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10-26-76 Eric Weber  
 10-29-76 Karl S. L. Leimer  
 11-8-76 Kyle Don Nelson  
 11-11-76 Evelyn Marie Rowland  
 11-15-76 Elbert T. Howell  
 12-6-76 Mildred E. Hutchins  
 12-6-76 Dana Ackerman  
 12-6-76 Anna Mae Lemke  
 12-7-76 Lee A. Mackey  
 12-15-76 Dave Kerr  
 12-16-76 Leo Hodges  
 12-16-76 Beatrice Meo  
 12-17-76 Jamie Holzen  
 12-17-76 Helen A. Nay  
 12-22-76 Charlene Kratzer  
 1-4-77 Margarite E. Perrigue  
 1-6-77 Ruby Jones Wren  
 1-11-77 Mrs. G. E. (Irma) Evans  
 1-17-77 Margaret Emde  
 2-4-77 Teddie M. Baird  
 2-7-77 Harry O'Keefe  
 2-7-77 Robert E. Taylor  
 2-15-77 Ilona Laszlo  
 2-15-77 James M. Scarborough  
 12-23-76 Evone Hollie  
 12-27-76 Mary Alice Sibel  
 12-30-77 Luella Kamphaus  
 1-18-77 Mabel Kays  
 1-18-77 Eleanor Elizabeth Timmons  
 1-20-77 Leo Elizabeth Boren  
 2-17-77 Robert Vernon McGuire  
 2-23-77 V. Kay Christopher  
 2-28-77 Juanita Wickham  
 3-8-77 Robert Perry Moss  
 3-28-77 Belle Gilliam  
 3-25-77 Lester Trilla  
 4-7-77 Bernadette Ortell  
 4-11-77 Frances Maureen Deal  
 4-12-77 Joy Marie Chastain  
 4-19-77 Billie Ann Jenkins

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DATE      PROCEEDINGS

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3-12-75 Filed Complaint  
 3-12-75 Filed prae for & issued summons  
 3-14-75 Ent hrg on plf's appl for a prel. inj.: (Daugherty) ve  
 (appl for prel. inj. cont'd at  
 (req. of plf; to be reset at  
 6-30-75 Filed plfs' Appl for Lv to File Amended Complaint  
 ws  
 6-30-75 Ent Order granting plfs' appl for lv to file amended  
 compl; dfts directed to ans or plead w/in 60 days  
 (Daugherty) ve ws  
 6-30-75 Filed plfs' Amended Complaint, adding plfs (see  
 caption)—ns shown  
 7-3-75 Filed plfs' Glen Rutherford, Gene W. Schneider &  
 Phyllis S. Schneider Appl for Temporary Order—ws  
 7-11-75 Ent Hrg on Temp Rest'g Order; statements made;  
 pltf presents appl w/test of witnesses & reses; plf's ex-  
 hibits 1-8 admitted; plf to file brief 7-15-75; case set  
 for hrg 7-18-75, 9:30 a.m. (Bohanon) sjb  
 8-14-75 Filed Findings of Fact & Conclusions of Law  
 (Bohanon)  
 8-29-75 Filed dfgts' Mtn to Dsms—ws (Memo in Supt  
 attached)  
 9-4-75 Filed Order Denying dfts' 2nd Mtn to Dsms filed 8-29-  
 75 (Bohanon) ws, sjb  
 10-3-75 Filed dfts' Mtn for Stay & Brief in Supt Thereof—  
 ws  
 10-6-75 Filed Order that dft's Mtn to Stay Ct's Order of  
 8-14-75 is denied (Bohanon) ws, sjb  
 10-8-75 Filed dft's Notice of Appeal from Order entered Aug  
 14, 1975 (record due CCofA 11-17-75)  
 10-10-75 Filed Order On Style of Case setting forth new  
 style of case (copies



## DATE

## PROCEEDINGS

- 11-24-76 Filed copy of CCofA's Opinion
- 1-24-76 Filed cert copy of CCofA's Mandate (judg affirmed insofar & only insofar as it grt the prel inj which we hold can cont in effect purs to 5 USC § 705; the cause is remanded to the USDC for thw [sic] WD of Ok for further proceedings consistent w/the views expressed in the opinion of this ct) (Holloway, McWilliams & Doyle) (CCA #75-1725) ws
- 12-30-76 Ent pretrial hearing—Statements made; pt stricken; case to be remanded to FDA for hrg. Ct to prepare order; dft to furnish ct & plfs information on file with FDA in 60 days (Bohanon) sjb
- 1-4-77 Filed Memorandum Opinion & Order<sup>3</sup> THAT dft FDA is enjoined & restrained fr preventing plfs' importation or interstate transp. of Laetrile for purposes of their own consumption under the terms of the F & D Act, incld'g ¶ 505(a) of the Act, 21 USC ¶ 355(a); that on remand an administ. record shall be developed w/i 120 dys herefrom & a copy shall be filed w/Clk of Ct & plfs w/i 30 days thereafter
- 3-18-77 Ent Hrg on plf appl. to clarify class (Evid. Hrg): statement made; plfs rests; dft presents obj. w/list of witness; parties rest; argmts hrg; plf to submit proposed order as to class; plf to file reply brief in 10 days; case to be set for further argument. (Bohanon) sjb
- 4-8-77 Filed Memo Opinion (Bohanon) ws
- 4-8-77 Filed *AND ENTERED* Order And Decree—THAT plf class is certified as encompassing all "terminally ill cancer patients"; the phrase "terminally ill cancer patient" refers to anyone who, in aff form as hereafter described is declared by a practicing physician (M.D.) to be terminally ill; such aff to incl things as more fully set out; that dfts, et al, are enj'd from impeding or preventing the importation & interstate transportation of laetrile by any members of the plf class or their duly designated agents; that such laetrile can be imported & utilized

## DATE

## PROCEEDINGS

- solely for the pers use & benefit of the plf class members; Clk to send, by reg mail, a cert copy hereof to ea dept administrator referred to herein (Bohannon) (COB #119) (Clerk) (Copies to parties—sjb)
- 5-9-77 Ent Hrg on Plf's Mtn for Contempt; stmts made; dft's Exh #1 adm; case passed to 5-10-77, 10am (Bohanon) sjb
- 5-10-77 Ent Hrg on clarification of Aff; stmts made; parties stip, ct files order (Bohanon) sjb
- 5-10-77 Filed Order on Aff & Ext; that the attchd aff will suffice & be sufficient for any cancer patient to have, receive & transport laetrile for his or her own use under the class action prev certified by the Ct on 4-8-77; the quantity of laetrile so had, received & transported shall be a 6 mo's supply not to exceed 750 tabs at 500 mlg per tab & 1500 cc's of injectable liquid; that the plf's mtn for contempt citation is moot; directed that the FDA disseminate a copy hereof & the attchd aff for the benefit of all concerned; that the req of the FDA for a 90 day ext to file it's adm record & report is grtd (Bohanon) ws
- 6-23-77 Filed Order that Dr. Mario A. Soto & Dr. Raul Morales Aceves are auth'd to execute affs as defined in the ct's order of 5-10-77, & that such affs will qualify the class member named in the aff to import & transport laetrile interstate under the terms & conditions of this ct's order of 5-10-77; that the FDA disseminate a copy hereof in the same manner & for the same purposes that the ct's order of 5-10-77 was disseminated (Bohanon) ws
- 7-12-77 Filed Order Allowing Certain Mexican Doctors to Execute Affs Identifying Plf Class Members—that Dr. Ernesto Contreras & Dr. Abel Mallado Prince are author'd to execute affs as defined in the ct's order of 5-10-77, & that such affs will qualify the class member named in the aff to import & transport laetrile interstate under the terms & conditions of the ct's 5-10-77, order; that the

## DATE

## PROCEEDINGS

FDA disseminate a copy of this order in the same manner & for the same purposes that the ct's order of 5-10-77, was disseminated; that dfts are granted 10 days w/in which to file any formal objs to this order; The Ct will hrg evid & oral arguments upon dft's req (Bohanon) w/s-sjb

8-4-77 Filed FDA's Administrative Record -ws consisting of 523 exhs, over 5000 pages

8-19-77 Filed Aff of Gerald M. Rachanow

8-31-77 Filed Supplemental Stip Order (Bohanon) (copies mailed-mc)

10-4-77 Filed Order—It is Stip between the plf & dft, U.S. Customs Service, that the 30 day grace period granted in parag 1 of the Supplemental Stip order filed 8-31-77 is extended to & including the 31st day of October, 1977. This extension is based upon representations that it has been impossible to obtain a customs bond even though diligent efforts have been made. See Aff of J. Franklin Salaman & letter of Ferd L Hershfield attached hereto as Exh A & B (Bohanon) (copies mailed & delivered-ih)

11-11-77 Filed Order—It is agreed by & between plf & dft, U.S. Customs Service, that the provisions of the Ct orders of 8-22-77 & 8-31-77 as they pertain to Customs' bonding requirements are hereby con't in effect until such time as the U.S. Dist Ct for the WD of Okla. rules upon the administrative record compiled by the Federal Food & Drug Administration & heretofore submitted to the Ct for judicial review (Bohanon) (copies mailed/delivered-wwm)

11-28-77 Filed Plf's Mtn for Preliminary Injunction -w/s

12-5-77 Filed Ct's Opinion (Bohanon) ns

12-12-77 Filed Notice of Appeal of dfts from final jdgmt entered Dec 5, 1977 (record due in CCofA 1-23-78)

IN THE UNITED STATES DISTRICT COURT  
FOR THE WESTERN DISTRICT OF OKLAHOMA

CIV—75-0218-D

[Filed March 12, 1975]

JUANITA IRENE STOWE and  
JIMMIE STOWE, Husband and Wife, PLAINTIFFS

vs.

UNITED STATES OF AMERICA and CASPER WEINBERGER,  
Secretary of Health, Education and Welfare, DEFENDANTS

COMPLAINT

For cause of action against the Defendants, Plaintiffs respectfully show to the Court:

I.

**PARTIES** The parties to this action and the  
**AND** facts which establish jurisdiction of  
**JURISDICTION:** this Court are:

1. *Plaintiffs:* Juanita Irene Stowe and Jimmie Stowe, husband and wife, are residents of Oklahoma.

2. *Defendants:* The United States of America (hereafter "USA"); and Casper Weinberger, Secretary of Health, Education and Welfare of the United States of America, (hereafter "SECRETARY"). Defendant, SECRETARY, supervises the United States Food and Drug Administration (hereafter "FDA").

3. The Plaintiffs are seeking relief under the Fifth and Fourteenth Amendments to the Constitution of the United States, under the Federal Food, Drug and Cosmetic Act, 21 USC 1/392, and the Administrative Procedure Act, 5 USC 701, Sec. 2. By reason of the actions of the SECRETARY as hereafter set forth, the rights of Plaintiffs, under the Constitution of the United States and under the above statutes have been violated, to the

extent that Plaintiffs are entitled to judicial relief in this cause; and this Honorable Court has jurisdiction over the parties to and subject matter of this action.

## II.

**RELATIONSHIP OF PARTIES:** By reason of action heretofore taken by the SECRETARY under and pursuant to 21 USC 355, a vitamin substance (B-17, also identified as Laetrile and Amygdalin) has been considered by the SECRETARY as a "new drug" within the definition of 21 USC 321(p); and the SECRETARY has, by a series of proceedings known to the SECRETARY, but unknown to Plaintiffs issued orders and regulations which preclude the dispensing of the said vitamin substance to persons suffering from cancer, upon the stated ground that the efficacy of the substance had not adequately been proven as a cancer remedy, and its use as a segment of anti-cancer therapy could have the result of precluding persons suffering from cancer from receiving other treatments recognized by the medical profession, and the use of other drugs approved by the SECRETARY.

## III.

**CAUSE OF ACTION:** Plaintiffs state that the Plaintiff, JUANITA IRENE STOWE, is suffering from cancer of the brain and lung; and is presently confined to Deaconess Hospital in Oklahoma City, Oklahoma, where she and the Plaintiff, JIMMIE STOWE, are incurring extensive financial obligations for her treatment with no hope of ultimate relief. Plaintiffs state that, because of the order and regulation of the SECRETARY, the Plaintiff, JUANITA IRENE STOWE, is unable to have nurses and doctors affiliated with the hospital administer to her B-17/Laetrile, which she has in her possession, and elects to use for the purpose of creating within her body a metabolic enzymatic reaction that would expose the cancer infested trophoblast cells to the destructive force of her body's white blood cells, thus permitting natural reactions of her body to control the out-of-phase reactions of the cancerous trophoblast cells in Plaintiff's body.

Plaintiffs state that the "liberty" protected by the Due Process Clause of the Fifth and Fourteenth Amendments to the Constitution of the USA would preclude the USA, acting by and through the SECRETARY, from invading the vital right of Plaintiff, JUANITA IRENE STOWE, to assert a freedom of choice in requesting the administration of an injection into her body of B-17/Laetrile for the purpose of accelerating her natural metabolic reactions, so long as such election of remedy on her part is taken with full knowledge of all scientific analyses presented by the SECRETARY, through the FDA. Plaintiffs further state that there has been no FDA analysis of B-17/Laetrile that would indicate lethal or even adverse effects upon the human body; but Plaintiff is denied her Constitutional right and liberty to obtain such treatment, solely by an FDA report that B-17/Laetrile had not yet been adequately proven as an effective anti-cancer therapy. With this information fully known to Plaintiffs, they would have a constitutional freedom of choice to request the administration of B-17/Laetrile; and an Order of this Honorable Court is sought to prevent the Defendant, SECRETARY, through the HEW and FDA, from precluding and restricting Plaintiff's liberty in a knowing freedom of choice to obtain Vitamin B-17/Laetrile treatment as above set forth. Plaintiffs state that the action of the SECRETARY, in arbitrarily and capriciously, through HEW and FDA, precluding and restricting Plaintiffs' liberty of a knowing freedom of choice to obtain Vitamin B-17/Laetrile treatment as set forth above are a violation of Plaintiffs' constitutional rights; and such action of the SECRETARY, in the arbitrary and capricious exercise of administrative judgment, to deny dying people a freedom of choice to obtain B-17/Laetrile treatments, when a pregnant [sic] has been recognized as having a freedom of choice to demand an abortion is a denial of Plaintiffs' constitutional rights including equal protection of the law, as well as denial of similar constitutional rights of other citizens of the USA.



## IV.

**REQUESTED** Plaintiffs state, that, by reason of the **RELIEF:** actions of the SECRETARY, as above set forth, and deprivation of Plaintiffs constitutional rights, Plaintiffs have no adequate remedy at law and are entitled to equitable relief as follows:

1. Judgment herein ordering and directing the SECRETARY to cease and desist from enforcement of order of FDA precluding the administration of Vitamin B-17/Laetrile to patients suffering from cancer.

2. In addition, and as ancillary relief, Plaintiffs are entitled to declaratory judgment under and pursuant to 28 USC 2201, as an enlargement upon the Plaintiffs' remedy against the SECRETARY, upon the ground of existence of an actual controversy within the jurisdiction of this Court, not involving Federal taxes; and Plaintiffs are entitled to a declaration and adjudication that the action of the SECRETARY in denying to Plaintiffs the right to have injections and dosages of Vitamin B-17/Laetrile is an unconstitutional denial and invasion of Plaintiffs' rights and liberties, under the Constitution of the USA.

3. Plaintiff, JUANITA IRENE STOWE, is now in a very critical condition, facing imminent death; and in order to assert her Constitutional rights to take advantage of the therapy to which she is entitled as an American Citizen, respectfully requests an early hearing for a temporary order to permit administration to her of B-17/Laetrile, both intervenuously and orally until this cause can be tried on its merits.

WHEREFORE, Plaintiffs pray judgment herein against the USA and the SECRETARY, as follows:

1. Judgment herein ordering and directing the SECRETARY to cease and desist from enforcement of order of FDA precluding the administration of Vitamin B-17/Laetrile to patients suffering from cancer.

2. In addition, and, as ancillary relief, Plaintiffs are entitled to declaratory judgment under and pursuant to 28 USC 220k, as an enlargement upon the Plaintiffs'

remedy against the SECRETARY, upon the ground of existence of an actual controversy within the jurisdiction of this Court, not involving Federal taxes; and Plaintiffs are entitled to a declaration and adjudication that the action of the SECRETARY in denying to Plaintiffs the right to have injections and dosages of Vitamin B-17/Laetrile is an unconstitutional denial and invasion of Plaintiffs' rights and liberties, under the Constitution of the USA.

3. That the Court fix an early date for a hearing of Plaintiffs' Application for temporary relief; and that Defendants be ordered to show cause why a temporary order should not be entered authorizing and directing the administration of B-17/Laetrile to Plaintiff, JUANITA IRENE STOWE, pending further order of the Court in this cause.

4. That Plaintiffs have such further judgment and relief, as may appear just and proper.

/s/ Clyde J. Watts  
CLYDE J. WATTS  
Attorney for Plaintiffs

## OF COUNSEL:

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IN THE UNITED STATES DISTRICT COURT  
FOR THE WESTERN DISTRICT OF OKLAHOMA

No. CIV—75-0218-D

[Filed June 30, 1975]

JIMMIE STOWE, Surviving husband of JUANITA STOWE,  
Deceased; GLEN L. RUTHERFORD; and GENE W. SCHNEI-  
DER and PHYLLIS S. SCHNEIDER, husband and wife, in-  
dividually and on behalf of a class composed of cancer  
victims and their spouses, who are responsible for the  
costs of treatment, PLAINTIFFS

vs.

UNITED STATES OF AMERICA and CASPER WEINBERGER,  
Secretary of Health, Education and Welfare, DEFENDANTS

AMENDED COMPLAINT

For cause of action against the Defendants, Plaintiffs  
respectfully show to the Court:

I.

**PARTIES**                   The parties to this action and the  
**AND**                       facts which establish jurisdiction of  
**JURISDICTION:**       this Court are:

1. **PLAINTIFFS:**

- a. Jimmie Stowe, surviving husband of Juanita Stowe,  
is a resident of the State of Oklahoma.
- b. Glen L. Rutherford is a resident of Conway Springs,  
Kansas.
- c. Gene W. Schneider and Phyllis S. Schneider, hus-  
band and wife, are residents of Tulsa, Oklahoma.

2. **DEFENDANTS:** The United States of America  
(hereafter "USA"); and Casper Weinberger, Secretary  
of Health, Education and Welfare of the United States  
of America, (hereafter "SECRETARY"). Defendant,

SECRETARY, supervises the United States Food and  
Drug Administration (hereafter "FDA").

3. The Plaintiffs are seeking relief under the Fifth  
and Fourteenth Amendments to the Constitution of the  
United States, under the Federal Food, Drug and Cos-  
metic Act, 21 USC 1/392, and the Administrative Pro-  
cedures Act, 5 USC 701, Sec. 2. By reason of the ar-  
bitrary and capricious actions of the SECRETARY as  
hereafter set forth, the rights of Plaintiffs, under the  
Constitution of the United States and under the above  
statutes have been violated to the extent that Plaintiffs  
are entitled to judicial relief in this cause; and, in ad-  
dition, Plaintiffs maintain this action as a class action  
under Rule 23, Federal Rules of Civil Procedure, as  
representative parties on behalf of all cancer victims, and  
their spouses who may be liable for the exorbitant costs  
of the "acceptable, modern curative methods (surgery  
and radiation)" to which the legislative type order of the  
SECRETARY, as published in the Federal Register, have  
restricted cancer victims. This class is so numerous that  
joinder of all members is impractical, questions of law  
and fact and claims and defenses are common to all, and  
the above Plaintiffs will fairly and adequately protect the  
interest of the class. With this action involving constitu-  
tional rights of the Plaintiffs, and the United States  
of America and its Secretary of Health, Education and  
Welfare parties hereto, this Honorable Court has juris-  
diction over the parties to and subject matter of this  
action.

II.

**RELATIONSHIP** By reason of action heretofore taken  
**OF PARTIES:** by the SECRETARY under and pur-  
suant to 21 USC 355, a vitamin substance (B-17, also  
identified as Laetrile and Amygdalin) has been con-  
sidered by the SECRETARY as a "new drug" within the  
definition of 21 USC 321(p); and the SECRETARY  
has, by a series of proceedings known to the SECRE-  
TARY, but unknown to Plaintiffs issued orders and regu-  
lations which preclude the dispensing of the said vitamin  
substance to persons suffering from cancer, upon the  
stated ground that the efficacy of the substance had not

adequately been proven as a cancer remedy, and its use as a segment of anti-cancer therapy could have the result of precluding persons suffering from cancer from receiving other treatments recognized by the medical profession, and the use of other drugs approved by the SECRETARY; and the United States of America, through its agents and appointed officials is now precluding the transportation in Interstate Commerce of Vitamin B-17/Laetrile to the prejudice and in violation of the constitutional rights of Plaintiffs and others included in the class represented by Plaintiffs and others included in the class represented by Plaintiffs in this class action, to purchase in interstate commerce, or otherwise, and have administered to them by medical practitioners the said Vitamin B-17.

### III.

**CAUSE OF ACTION:** Plaintiffs state that the Plaintiff, JUANITA IRENE STOWE, was suffering from cancer of the brain and lung; and was confined to Deaconess Hospital in Oklahoma City, Oklahoma, where she and the Plaintiff, JIMMIE STOWE, were incurring extensive financial obligations for her treatment with no hope of ultimate relief. Plaintiffs state that, because of the order and regulation of the SECRETARY, the Plaintiff, JUANITA IRENE STOWE, was unable to have nurses and doctors affiliated with the hospital administer to her B-17/Laetrile, which she had in her possession, and elected to use for the purpose of creating within her body a metabolic enzymatic reaction that would expose the cancer infested trophoblast cells to the destructive force of her body's white blood cells, thus permitting natural reactions of her body to control the out-of-phase reactions of the cancerous trophoblast cells in her body. Before she was able to obtain such treatment with B-17/Laetrile, JUANITA IRENE STOWE died; and Plaintiff, JIMMIE STOWE, incurred extensive medical, hospital and burial expenses, many of which are still unpaid.

The Plaintiff, PHYLLIS S. SCHNEIDER, is now suffering from terminal cancer; and, unless she is permitted to receive Vitamin B-17/Laetrile treatments, she

faces the same fate as JUANITA STOWE. The Plaintiff, GLEN L. RUTHERFORD, has been treated with Vitamin B-17/Laetrile for approximately four (4) years, and his cancer is temporarily dormant; but, with his supply of Vitamin B-17/Laetrile blocked by the refusal of the Defendant, SECRETARY, to permit transport of Vitamin B-17/Laetrile in interstate commerce, he faces a re-occurrence and escalation of his cancer, with probably fatal results.

Plaintiffs state that the "liberty" protected by the Due Process Clause of the Fifth and Fourteenth Amendments to the Constitution of the USA would preclude the USA, acting by and through the SECRETARY, from invading the vital right of Plaintiffs to assert a freedom of choice in requesting the administration of an injection into the bodies of the said cancer victims B-17/Laetrile for the purpose of accelerating their natural metabolic reactions, so long as such election of remedy on the part of the cancer victim is taken with full knowledge of all scientific analyses presented by the SECRETARY, through the FDA. Plaintiffs further state that there has been no FDA analysis of B-17/Laetrile that would indicate lethal or even adverse effects upon the human body; but Plaintiffs and other cancer victims, present and future are denied their Constitutional right and liberty to obtain such treatment, solely by an FDA report that B-17/Laetrile had not yet been adequately proven as an effective anti-cancer therapy. With this information fully known to Plaintiffs, and available to other cancer victims, they would have a constitutional freedom of choice to request the administration of B-17/Laetrile; and an Order of this Honorable Court is sought to prevent the Defendant, SECRETARY, through the HEW and FDA, from precluding and restricting Plaintiffs' liberty, with a knowing freedom of choice, to obtain Vitamin B-17/Laetrile treatment as above set forth. Plaintiffs state that the action of the SECRETARY, in arbitrarily and capriciously, through HEW and FDA, precluding and restricting Plaintiffs' liberty of a knowing freedom of choice to obtain Vitamin B-17/Laetrile treatment as set forth above are a violation of Plaintiffs' constitutional rights as well as the constitutional rights of the entire



class of cancer victims, present and future, and such action of the SECRETARY, in the arbitrary and capricious exercise of administrative judgment, to deny dying people a freedom of choice to obtain B-17/Laetrile treatments, when a pregnant woman has been recognized as having a freedom of choice to demand an abortion, is a denial of Plaintiffs' constitutional rights including equal protection of the law, as well as denial of similar constitutional rights of other citizens of the USA.

#### IV.

*REQUESTED* Plaintiffs state, that by reason of the *RELIEF*: actions of SECRETARY, as above set forth, and deprivation of Plaintiffs' constitutional rights, Plaintiffs have no adequate remedy at law and are entitled to equitable relief as follows:

1. Judgment herein ordering and directing the SECRETARY to cease and desist from enforcement of order of FDA precluding the administration of Vitamin B-17/Laetrile to patients suffering from cancer.

2. In addition, and as ancillary relief, Plaintiffs are entitled to declaratory judgment under and pursuant to 28 USC 2201, as an enlargement upon the Plaintiffs remedy against the SECRETARY, upon the ground of existence of an actual controversy within the jurisdiction of this Court, not involving Federal taxes; and Plaintiffs are entitled to a declaration and adjudication that the action of the SECRETARY in denying to Plaintiffs the right to have injections and dosages of Vitamin B-17/Laetrile is an unconstitutional denial and invasion of Plaintiffs' rights and liberties, under the Constitution of the United States of America.

3. The former Plaintiff, JUANITA IRENE STOWE, passed away before she was able to assert her constitutional rights before this Honorable Court; and the Plaintiff, PHYLLIS S. SCHNEIDER, faces a similar fate. In order to assert her constitutional rights to take advantage of the therapy to which she is entitled as an American Citizen, the said Plaintiff respectfully requests an early hearing for a temporary order to permit administration

to her of B-17/Laetrile, both intervenuously and orally until this cause can be tried on its merits.

WHEREFORE, Plaintiffs pray judgment herein against the USA and the SECRETARY, as follows:

1. Judgment herein ordering and directing the SECRETARY to cease and desist from enforcement of order of FDA precluding the administration of Vitamin B-17/Laetrile to patients suffering from cancer.

2. In addition, and, as ancillary relief, Plaintiffs are entitled to declaratory judgment under and pursuant to 28 USC 220K, as an enlargement upon the Plaintiffs' remedy against the SECRETARY, upon the ground of existence of an actual controversy within the jurisdiction of this Court, not involving Federal taxes; and Plaintiffs are entitled to a declaration and adjudication that the action of the SECRETARY in denying to Plaintiffs the right to have injections and dosages of Vitamin B-17/Laetrile is unconstitutional denial and invasion of Plaintiffs' rights and liberties, under the Constitution of the United States of America.

3. That the Court fix an early date for a hearing of Plaintiff, PHYLLIS S. SCHNEIDER, Application for Temporary Relief; and that Defendants be ordered to show cause why a temporary order should not be entered authorizing the administration of B-17/Laetrile to Plaintiff, PHYLLIS S. SCHNEIDER, pending further order of the Court in this cause.

4. That Plaintiffs have such further judgment and relief, as may appear just and proper.

/s/ Clyde J. Watts  
CLYDE J. WATTS  
Attorney for Plaintiffs

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IN THE UNITED STATES DISTRICT COURT  
FOR THE WESTERN DISTRICT OF OKLAHOMA

No. CIV-75-0218-B

[Filed August 14, 1975]

JIMMIE STOWE, Surviving husband of JUANITA STOWE,  
Deceased; GLEN L. RUTHERFORD; and GENE W. SCHNEI-  
DER and PHYLLIS S. SCHNEIDER, husband and wife, in-  
dividually and on behalf of a class composed of cancer  
victims and their spouses, who are responsible for the  
costs of treatment, PLAINTIFFS

vs.

UNITED STATES OF AMERICA and CASPER WEINBERGER,  
Secretary of Health, Education and Welfare, DEFENDANTS

ORDER

Based upon the Findings of Fact and Conclusions of  
Law filed herein this day,

IT IS ORDERED, ADJUDGED AND DECREED that  
the defendant United States of America and defendant  
Casper Weinberger, Secretary of Health, Education and  
Welfare, his successors, and each of them and their rep-  
resentatives, agents, servants and employees be enjoined  
from preventing the plaintiff Glen L. Rutherford from  
purchasing and moving in interstate commerce, and hav-  
ing for his own personal use, not for sale, barter or to be  
given away to any other person an amount not in excess  
of a six-months' supply of Vitamin B17 or laetrile, the  
prescribed daily requirement being "2 pills (500 mg  
each) a day and 3 Wobe-Mugos enzymes a day." A  
six-months' supply, therefore, of each of these drugs  
would amount to 365 laetrile pills and 547 Wobe-Mugos  
enzymes.

IT IS FURTHER ORDERED, ADJUDGED AND DE-  
CREED that the plaintiff Glen L. Rutherford give ad-

vance notification to the defendants' attorney of record  
of the date, place and quantity of his transportation  
in interstate commerce of such amount of laetrile as  
above authorized. Such quantity shall further be de-  
clared to the immigration authorities, and custom or tax,  
if any, due thereon shall be paid.

IT IS FURTHER ORDERED, ADJUDGED AND  
DECREED that the above and foregoing Order be, and  
the same is hereby stayed for a period of sixty (60)  
days from this date.

Dated this 14th day of August, 1975.

/s/ Luther Bohanon  
United States District Judge

UNITED STATES DISTRICT COURT  
W.D. OKLAHOMA

No. CIV-75-0218-B

GLEN L. RUTHERFORD, PLAINTIFF, INTERVENOR  
and

JIMMIE STOWE and GENE SCHNEIDER, Individually and  
on behalf of a class composed of cancer victims and  
their spouses, who are responsible for the costs of  
treatment, ORIGINAL PLAINTIFFS

v.

UNITED STATES OF AMERICA and CASPER WEINBERGER,  
Secretary of Health, Education and Welfare, DEFENDANTS

Aug. 14, 1975  
As Amended Oct. 10, 1975

FINDINGS OF FACT AND  
CONCLUSIONS OF LAW

BOHANON, District Judge.

The case was called and the parties announced ready for trial on plaintiff's Amended Complaint insofar as it pertains to a temporary injunction, plaintiff praying that this Court order and direct the Secretary of Health, Education and Welfare (HEW), of which the Federal Drug Administration (FDA) is a branch, to desist from precluding the administration of Vitamin B17 or laetrile to patients in the United States suffering from cancer.

The plaintiffs seek relief under the Fifth Amendment to the Constitution of the United States from the provisions of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. §§ 1-392 alleging that by reason of the arbitrary and capricious acts of the Secretary the rights of the plaintiffs, under the Constitution of the United States and under the statutes herein involved, have been violated wherein plaintiffs are entitled to judicial relief and

are entitled to maintain this action as a class action under Rule 23 Federal Rules of Civil Procedure.

Plaintiff Glen L. Rutherford testified that he became ill with cancer in the summer and fall of 1971 and that he was examined by local medical doctors who concluded that he was suffering from cancer. Thereafter he was sent to J. Walker Butin, M.D. of the Wichita Clinic, Wichita, Kansas, for examination and diagnosis.

A number of letters were written by the doctors treating Mr. Rutherford, none of which letters were written in contemplation of this legal action. Such letters which comprise Plaintiffs' Exhibit 1 are in pertinent part as follows:

On November 30, 1971, J. Walker Butin, M.D., of the Wichita Clinic, wrote to Eugene C. McCormick, M.D. of Wellington, Kansas, regarding plaintiff Rutherford:

"Dear Dr. McCormick:

*. . . We found the source of his bleeding on sigmoidoscopy. A large polyp is present at 15 cm. from the anal sphincter. It prolapses down and fills the lumen at this point. I was able to biopsy it and the specimen was sent to the Associated Laboratories; we should have a report in two or three days.*

*My proposal is that he be seen by Dr. Bartlett here with a sigmoidoscopy to see if it might be possible to remove this polyp from below by fulguration. At the moment I think it probably is too large for anything but surgical removal, but if it is okay with you and the patient, we will schedule him to see Dr. Bartlett for his opinion.*

\* \* \* \*

*At the moment the arrangement is that he will call us back for the biopsy report in 72 hours, and we will arrange follow-up with Dr. Bartlett and will get his polyp out in the near future."*



Dr. Butin again wrote on December 4, 1971:

*"Dear Dr. McCormick:*

*Here is the latest followup on Mr. Rutherford.*

*He was seen by Dr. Bartlett yesterday, December 3, and was advised that, because of the biopsy showing an invasive adenocarcinoma in the polyp, he should have open operation.*

*Consequently, he is scheduled to enter Wesley Medical Center on December 10, 1971, for preoperative colon prep and apparently will have surgery several days later, possibly on Tuesday, December 14. The lesion is at about 15 centimeters which is an area where abdominoperineal resection is sometimes necessary. However, it is our hope that he can have an anterior resection with reformation of the normal bowel continuity possible."*

On February 28, 1972, Dr. Butin wrote to Dr. Price of Wellington, Kansas:

*"Dear Dr. Price:*

*Mr. Rutherford reported to the Wichita Clinic on November 1, 1971, with a history of aching in the left upper quadrant and bloody stools. On examination, he was rather tender in the middle and left upper abdomen, but there were no specific findings of mass or palpable organs.*

*Sigmoidoscopy of 15 cm revealed a large prolapsing polyp which appeared pedunculated. This was biopsied and the path report described invasive, well differentiated adenocarcinoma.*

*He saw Dr. Bartlett on December 3, 1971, and was scheduled to enter Wesley on December 10 for surgery. He was told that removal of the rectum might be necessary but that it would be saved, if possible. As you are well aware, he has not reported for this surgery.*

\* \* \*

*We would certainly urge Mr. Rutherford not to delay any longer than the three months, which have already been lost, in the treatment of his polyp. This should be an entirely curable lesion, if removal is performed without delay."*

The plaintiff Glen L. Rutherford testified that he was tremendously upset and concerned about the prospects of surgery and the results thereof and that he went to Centro Medico Del Mar in Tijuana, Mexico, for examination and treatment shortly after the report from Dr. Butin was made to him. He stated that at Centro Medico Del Mar he was treated with Vitamin B17 or laetrile for a period of weeks and that through this treatment his condition was cured; that he has returned to his home and has been working at all times since, averaging 10 to 12 hours per day. Mr. Rutherford stated that he has no ill effects of the cancer. However, he feels that without the continued use of laetrile as diagnosed by Dr. Carlos Lopez he faces the prospect of escalation of the lethal cancer cells and thus is seeking relief in this Court for the privilege of buying laetrile for his own use and not for sale or barter to others.

Carlos Lopez, M.D., of the Centro Medico Del Mar, Tijuana, Mexico, wrote on August 8, 1974:

*"Re: Glen L. Rutherford*

*This 57 year old white male came to us for a checkup on June 27, 1974. His past history revealed rectal bleeding in the summer of 1969. Saw a doctor at this time and was told it was diverticulitis. He was referred to Dr. Butin in November 1971. After a sigmoidoscopy they found a large polyp and a biopsy was performed. This showed invasive adenocarcinoma. Scheduled for surgery December 10, 1971, but did not show up.*

*Came first time to our hospital on December 21, 1971. After treatment here the bleeding had quit and we cauterized the remaining polyp. The treatment was Amygdalin i.v. (3 grams) plus proteolytic enzymes. He took home oral Bly and Wobe-Mugos enzymes.*

*Now he has come again for a checkup. Physical examination unremarkable . . .*

*Chest X-Rays show a doubtful nodule in the left lung in the R.M.L. portion (lingula). The rest of the studies were negative. Barium enema did not show any tumors in the rectum, but showed a diverticulitis inflammation of some of them and others with fecal matter.*

*We asked him to continue on same dosage of B17 2 pills (500 mg each) a day and 3 Wobe-Mugos enzymes a day."*

The Court is compelled to find from the testimony and the exhibits that plaintiff Glen L. Rutherford was in late 1971 suffering from invasive adenocarcinoma and that by the use of laetrile, B17 or amygdalin (all being the same drug) his condition was cured, as there is no evidence to the contrary.

The Court finds that plaintiff's Exhibit 2 is a letter from Mr. Rutherford's supplier of B17 or laetrile stating plaintiff's last order of laetrile was seized. It states that the carrier is in jail facing a \$10,000 fine and five years in prison for his efforts to furnish Mr. Rutherford his 1975 supply of laetrile. The writer says that the clinic cannot be responsible and that therefore there will be no more mail orders of laetrile in the future.

The Court finds that the plaintiff Rutherford is not free to have shipped to him, nor is he free to directly purchase and bring back to the United States from Mexico quantities of laetrile for preventive treatment of his cancer. To do so would violate the law and would subject him to criminal prosecution.

21 U.S.C. § 355 provides:

*"(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug."*

In this connection the Court finds that laetrile has been in use for a number of years in Mexico and other nations around the world; that the FDA has by its

regulations made it impossible for the common man to have an application processed through FDA so that said agency would either approve or disapprove the drug known as laetrile. The Court finds that Congress intended by 21 U.S.C. § 355 that the FDA would on its own initiative and in good faith approve or disapprove the use of laetrile, thereby allowing the courts jurisdiction of the subject matter.

The Court finds that the FDA has abdicated its duty to make a clear determination of whether the drug laetrile should or should not be placed in commerce though the drug has been in use for many years and thousands of persons have been treated with it.

The Court finds from the record, testimony and exhibits that laetrile is not lethal in any sense of the word. It is not harmful to the human body and when used in proper amounts under proper control and supervision can effect relief from cancer disease to the satisfaction of many who are privileged to use the same.

The Court further finds from the record that the plaintiff Rutherford herein and those similarly situated have been denied this right of choice in using B17 or laetrile without just cause on the part of the Secretary of HEW and its agency FDA.

Inaction by the FDA constitutes the crux of plaintiff's procedural dilemma, and the question arises relevant to plaintiff's request for equitable relief, as to whether an interpretation or construction of § 355 authorizes such inaction and is in keeping with the Congressional intent the statute embodies. Section 355 states in part:

*"(c) Within one hundred and eighty days after the filing of an application . . . the Secretary shall either—*

*(1) approve the application . . . or*

*(2) give . . . notice of an opportunity for a hearing . . .*

*(d) If the Secretary finds, after due notice to the applicant . . . that (1) the investigations . . . do not*

*include adequate tests . . . ; (2) the results . . . show that such drug is unsafe . . . or do not show that such drug is safe . . . ; (3) the methods used . . . or (5) . . . there is a lack of substantial evidence that the drug will have the effect it purports . . . he shall issue an order refusing to approve the application."*  
(Emphasis Added)

It can be seen that the statute allows but two alternatives: the issuance of an order approving the application or the issuance of an order refusing to approve the application. The evidence does not reflect the Secretary to have done either. Without a refusal order, the plaintiff may not invoke the jurisdictional grant of § 355 giving jurisdiction to the Court of Appeals where applicant resides or the United States Court of Appeals for the District of Columbia. This section permits the United States Court of Appeals for the Tenth Circuit to take original jurisdiction.

Thus the statutory duty has not been carried out and cancer victims have thereby been placed in limbo with regard to laetrile, unable to invoke the jurisdiction of the courts. Since the Secretary has failed to act, the Court must act on behalf of this plaintiff who has been adversely affected by such failure. Congress has not legislated a statute which can be used by silence and inaction to still the clamor and demands of citizens, especially those nearly 1,000 who die each day of cancer.

Since the FDA has failed to act in contemplation of what Congress intended by § 355, the Court concludes and finds the HEW and FDA have in fact disapproved the use of laetrile and that this Court does have jurisdiction for want of action on the part of such governmental agencies.

Michael L. Culbert states in his book, *Vitamin B17*, published by Arlington House, New Rochelle, New York, at page 81:

*"In April 1970 the Food and Drug Administration assigned IND (Investigative New Drug) application 6734 to the McNaughton Foundation, based in California, to test amygdalin-Laetrile, a move which*

*would have given the foundation permission to obtain supplies of the 'investigational drug' and to initiate clinical studies. Then, ten days later, permission was suddenly revoked by the FDA, allegedly at the behest of the then surgeon general Jesse Steinfeld, a California physician involved in the California Medical Association ban on the compound in the 1950s. Dr. Charles C. Edwards, FDA commissioner, stated on June 9, 1970:*

*As with all 'cancer' drugs the review of the IND was expedited . . . This review was completed on April 27, 1970, 21 days from the date of receipt. The review disclosed a number of serious preclinical deficiencies.*

*On April 28, 1970, a 10-day pretermination notice was issued detailing the deficiencies in the notice, and the sponsor was notified by wire to immediately cease clinical studies. The sponsor was allowed 10 days in which to either request a conference or to correct the deficiencies which were brought to his attention.*

*Since the sponsor did neither, the IND was terminated on May 12, 1970."*

The Court finds that the plaintiff Rutherford and those similarly situated are wholly without means or resources to comply with the provisions of 21 U.S.C. § 355(b) and that for the plaintiff Rutherford and those similarly situated to be denied the freedom of choice for treatment by laetrile to alleviate or cure their cancer, was and is a deprivation of life, liberty or property without due process of law guaranteed by the Fifth Amendment to the Constitution of the United States.

In *Abbott Laboratories v. Gardner*, 387 U.S. 136, 87 S.Ct. 1507, 18 L.Ed.2d 681 (1967) where a similar problem confronted the Courts, the Supreme Court recognized that the issue was a proper subject for judicial resolution, where a hardship from precluding Court consideration was demonstrated. Certainly hardship is revealed in this case where plaintiffs are afflicted with cancer and



are denied their choice of treatment by surgery, radiation cobalt treatments or by laetrile. The Supreme Court in the above cited case makes the following comments:

*"The first question we consider is whether Congress by the Federal Food, Drug, and Cosmetic Act intended to forbid pre-enforcement review of this sort of regulation . . . . The question is phrased in terms of 'prohibition' rather than 'authorization' because a survey of our cases shows that judicial review of a final agency action by an aggrieved person will not be cut off unless there is persuasive reason to believe that such was the purpose of Congress. . . .*

*. . . The Government relies on no explicit statutory authority for its argument that pre-enforcement review is unavailable . . . .*

*. . . 'any citizen aggrieved by any order of the Secretary, who contends that the order is invalid, may test the legality of the order by bringing an injunction suit against the Secretary, or the head of the Bureau, under the general equity powers of the court.'*

\* \* \* \*

*This is also a case in which the impact of the regulations upon the petitioners is sufficiently direct and immediate as to render the issue appropriate for judicial review at this stage."*

In *Roe v. Wade*, 410 U.S. 113, 93 S.Ct. 705, 35 L.Ed.2d 147 (1973), the Court extended to a pregnant woman the right of "privacy" which included the right to demand an abortion, contrary to a state criminal statute, even though the Constitution does not explicitly mention any right of privacy. The Court, nevertheless, extended such constitutional right to a pregnant woman in the following language:

*"This right of privacy, whether it be founded in the Fourteenth Amendment's concept of personal liberty and restrictions upon state action, as we feel it is, or, as the District Court determined, in the Ninth Amendment's reservation of rights to the*

*people, is broad enough to encompass a woman's decision whether or not to terminate her pregnancy."*

Justice Stewart in a concurring decision commented:

*"Several decisions of this Court make clear that freedom of personal choice in matters of marriage and family life is one of the liberties protected by the Due Process Clause of the Fourteenth Amendment."*

The Court concludes that in cases where jurisdiction is clearly shown, the Court may balance the various factors appropriate to the requested relief. Here the evidence is convincing that irreparable harm to the plaintiff overshadows the possible harm to the defendants or other interested persons. The plaintiff Rutherford's cancer is presently dormant; however, there is danger of recurrence of the cancer unless plaintiff continues to receive treatment. In addition, the plaintiff in order to have and use B17 or laetrile is subjecting himself and his agent to criminal prosecution should plaintiff contravene prohibitions set out in § 355 by making what plaintiff feels is a life versus law decision, *Continental Oil Co. v. Frontier Ref. Co.*, 338 F.2d 780 (C.A. 10, 1964).

The Court concludes that it has jurisdiction under 28 U.S.C. § 1337 where provision is made for jurisdiction of proceedings arising under any Act of Congress regulating commerce and where the prohibiting language of § 355 of the Pure Food and Drug Act stems from and has to do with commerce powers of the United States. It has been shown that the plaintiff here is precluded from transporting laetrile or B17 in commerce. See *Schatte v. International Alliances of Theatrical Stage Employees & Moving Picture Operators of U.S. and Canada*, 70 F.Supp. 1008 (D.C. Cal. 1947), *aff'd* 165 F.2d 216 (9 Cir.) *cert. denied* 334 U.S. 812, 68 S.Ct. 1018, 92 L.Ed. 1743.

The Court finds from the evidence that laetrile is not a toxic or harmful substance if used in proper dosage but is on the other hand an alternative treatment of cancer which can be used in lieu of surgery or radiation cobalt.

After plaintiff presented its evidence and rested, the Court inquired of defendant counsel if defendant had any evidence to offer and the reply was in the negative. Thereafter the following colloquy took place:

*"MR. GELLER: On the jurisdictional issue, if the Court finds that there is no jurisdiction, the Court could, I believe, allow them to take that up on appeal. If the Court finds there is no jurisdiction, then there is no lawsuit anyway and I think that would be a final judgment.*

\* \* \*

*MR. GELLER: If the Court did grant a temporary injunction, we would take a stay and we would take it up to the Circuit as soon as possible for review by the Tenth Circuit Court of Appeals.*

*THE COURT: Suppose I would enter an injunction in the nature of a permanent injunction and stay it until you could take it up on appeal.*

*MR. GELLER: Assuming the Court would be found to have jurisdiction, then what the Court would in essence be doing would be saying that this drug is perfectly acceptable to be used and would be an implicit finding by the Court that this drug is effective for the use for which it is intended and perfectly safe, and I think under the state of the evidence before the Court it is not possible to make such a finding. The Government has not presented nor has it been aware of the necessity to do so in the nature of a hearing on the merits. It has been our understanding that this is temporary to allow one individual to receive this and we have attacked it solely on the jurisdictional ground."*

From all of the facts and circumstances in this case the Court concludes that proper equitable injunctive relief should be granted and a proper Order will accordingly be filed.

UNITED STATES COURT OF APPEALS  
TENTH CIRCUIT

No. 75-1725

GLEN L. RUTHERFORD, PLAINTIFF INTERVENOR-APPELLEE

and

JIMMIE STOWE and GENE SCHNEIDER, Individually and on behalf of a class composed of cancer victims and their spouses, who are responsible for the cost of treatment, ORIGINAL PLAINTIFFS-APPELLEES

v.

UNITED STATES OF AMERICA and DAVID MATHEWS,  
Secretary of Health, Education and Welfare,  
DEFENDANTS-APPELLANTS

Argued and Submitted July 30, 1976

Decided Oct. 12, 1976

Before HOLLOWAY, McWILLIAMS and DOYLE,  
Circuit Judges.

WILLIAM E. DOYLE, Circuit Judge.

The Department of Health, Education and Welfare here seeks review and reversal of a judgment of the District Court for the Western District of Oklahoma which temporarily enjoined the Department, and particularly the Food and Drug Administration, from preventing appellee Rutherford from obtaining a supply of a controversial cancer drug called Laetrile for his own use. An order was issued on behalf of Rutherford which allowed him to purchase and transport in commerce a six months' supply of Laetrile and accompanying drugs. In the course of this order the trial court found that Laetrile was not toxic and further found that if properly administered it would "effect relief from cancer disease to the satisfaction of many who are privileged to use the same." The court also ruled that the FDA

was required under the law to approve or disapprove Laetrile as a cancer treatment and that it had neglected its duty in this regard. The judge also held that the new drug application requirements contained in the Food and Drug Act, Section 505(b), 21 U.S.C. Section 355(b), violated the Fifth Amendment due process clause in that they prescribed expensive procedures which could not be carried out by persons in the position of Rutherford.<sup>1</sup>

The government seeks reversal on statutory grounds:

First, that it (FDA) has no duty to approve a new drug unless a so-called new drug application is submitted to it.

Second, that it is not empowered to determine the safety and efficiency of Laetrile.

Third, that the court exceeded its authority in issuing the injunction, the effect of which was to block the enforcement of an Act of Congress without convening a three-judge court, 28 U.S.C. Sections 2282 and 2284.

We need not review the judge's ruling that Laetrile is an effective treatment for cancer or that Laetrile is not toxic or that the new drug application provision is unconstitutional. We confine ourselves to the issue whether the so-called new drug procedure constitutes, as H.E.W. contends, the only legal route that is available for testing the drug for harmfulness or harmlessness. So considered, we are of the opinion that the question whether this is a new drug presents a mixed question of fact and law which should be fully tried. As it is, the FDA's record is grossly inadequate and consists merely of a conclusory affidavit of an official of the FDA which

<sup>1</sup> The suit was initially brought as an individual action only by a cancer patient, Juanita Stowe, and her husband on March 12, 1975. Judge Daugherty heard and denied Mrs. Stowe's request for a preliminary injunction allowing her to obtain Laetrile on March 14, 1975. Mrs. Stowe subsequently died. An amended complaint was filed June 30, 1975 by two other cancer patients, Rutherford and Phyllis Schneider, and Mrs. Schneider's husband, on behalf of cancer victims and their spouses. Mrs. Schneider died before the hearing on a preliminary injunction held July 11 and 18, 1975, before Judge Bohanon. There has been no certification of the lawsuit as a class action.

in effect declares that it is a new drug because the FDA says it is and thus is subject to all of the statutory vagaries of such a designation.

## I.

As we view it, the reason that the Food and Drug Administration is anxious to classify Laetrile as a new drug is so as to bring it within the new drug certification procedures of the Food, Drug and Cosmetics Act. Section 505(a) of the Act, 21 U.S.C. Section 355(a). This provision bars the introduction into interstate commerce of a new drug without an approved new drug application having been filed pursuant to the Act just cited. The Secretary is required to review the application within a specified period on the criteria of safety and effectiveness as demonstrated by "adequate and well-controlled investigations." Such an application is reviewable directly in the court of appeals. The plaintiff-appellee's position on this is that Laetrile escapes the clutches of this Act by being a food rather than a drug, or even if it is a drug it is not a new drug.

## A.

It is unnecessary to linger and dwell on the subject whether it is a food or a drug inasmuch as this is not determinative. Appellee argues that it is in the nature of a diet supplement or a vitamin, but the cases recognize that even if a substance is also a food it may be subjected to the requirements of the Act if it is used in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals.<sup>2</sup> Intended use is an important aspect in the determination whether it is a

<sup>2</sup> *Kordell v. United States*, 335 U.S. 345, 69 S.Ct. 106, 93 L.Ed. 52 (1948) (mixture of minerals, vitamins, and herbs); *Seven Cases v. United States*, 239 U.S. 510, 518, 36 S.Ct. 190, 60 L.Ed. 411 (1916) (alcoholic solution); *United States v. Allan Drug Corp.*, 357 F.2d 713 (10th Cir.), cert. denied, 385 U.S. 899, 87 S.Ct. 203, 17 L.Ed.2d 131 (1966) (vitamin supplements offered as acne cure); *United States v. Millpax, Inc.*, 313 F.2d 152, 153-54 (7th Cir. 1963), cert. denied, 373 U.S. 903, 83 S.Ct. 1291, 10 L.Ed.2d 198 (1963) ("iron tonic"); *United States v. 250 Jars of U.S. Fancy Pure Honey*, 218 F.Supp. 208 (E.D. Mich 1963), aff'd, 344 F.2d 288 (6th Cir. 1965) (honey sold for therapeutic purposes).



drug. See *Hanson v. United States*, 417 F.Supp. 30 (D. Minn. 1976).

Unquestionably Laetrile is *intended* at least as a treatment for cancer, so the likelihood that Rutherford can demonstrate that it is not a drug at all appears slim. Hence if this were the only issue to sustain the injunction it would be unnecessary to proceed further.

## B.

### THE QUESTION WHETHER LAETRILE IS A NEW DRUG

Rutherford vigorously argues that even if it is a drug it is not a new one, and therefore, it is exempt from the thicket which results from seeking to comply with Section 505(a) of the Act. A new drug is defined in Section 201(p) of the Act, 21 U.S.C. Section 321(p) as follows:

(p) The term "new drug" means—

(1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this chapter it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to

a material extent or for a material time under such conditions.

Essentially, then, a new drug is a substance which may or may not be generally recognized by scientific experts as safe and effective for use under the conditions prescribed, recommended or suggested in the labeling thereof. A substance is not regarded as a new drug if at any time prior to 1962, the date of the New Drug Amendment in question, it was subject to the Act of June 30, 1906, as amended. The effect of this definition is that there is a twofold grandfather clause exemption which is capable of removing Laetrile from the new drug category even if it is not recognized by the experts as being safe and effective which, by the way, does not say that it is unsafe and ineffective. The first of these grandfather exemptions comes from transitional provisions attached to the 1962 Amendments to the Food, Drug and Cosmetic Act of 1938. The second grandfather exemption arises from provisions attached to the 1938 Act when it superseded the original Food and Drug Act of 1906.

#### 1. Whether the Transitional Provisions Between the 1938 and 1962 Acts Applies

Prior to the 1962 Amendment the only prerequisite for a drug to avoid classification as a new drug was recognition that it was safe. But the 1962 Amendment added the requirement of "effectiveness." See Act of October 10, 1962, Pub. L. 87-781, Section 102(a)(1). One of the transitional provisions enacted in 1962 was as follows:

In the case of any drug which, on the day immediately preceding the enactment date (October 10, 1962), (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force (21 U.S.C. Section 321(p)), and (C) was not covered by an effective (new drug) application under 505 of that Act (21 U.S.C. Section 355), the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use

under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day. Pub. L. 87-781, Section 107(c) (4), *reprinted at 21 U.S.C. Section 321 note.*

The effect of this is that if on October 9, 1962, Laetrile was "marketed before 1962 for exactly the same uses for which it is presently being sold and was generally recognized by qualified experts as safe for those uses, it is exempt under this grandfather clause from the test of general recognition by experts as being both safe and effective for its claimed uses." *Tyler Pharmacal Distributors, Inc. v. United States Dep't of HEW*, 408 F.2d 95, 99 (7th Cir. 1969). See also *United States v. Allan Drug Corp.*, 357 F.2d 713, 717 (10th Cir.), *cert. denied*, 385 U.S. 899, 87 S.Ct. 203, 17 L.Ed.2d 131 (1966). The present record does not reveal how Laetrile was marketed before the passage of the 1962 Amendment nor does it tell us whether it was recognized as safe. We are mindful, of course, that the cause was not tried on its merits and hence these questions were not considered on preliminary injunction. They should, however, be taken up when the cause is remanded.

## 2. Whether the Other Transitional Provision as Between the 1906 and 1938 Acts Applies

In essence this exemption provides that a drug not recognized by qualified experts as "safe and effective"

shall not be deemed to be a "new drug" if at any time prior to the enactment of this chapter (the 1938 Act) it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use.

21 U.S.C. Section 321(p) (1).

The effect of this above quoted provision is to exempt from the new drug classification any drug which was marketed before the Food, Drug and Cosmetic Act of 1938 was enacted and which was covered by the predecessor Act, that is, the Food and Drugs Act of 1906 (as

long as the prescribed conditions for its use are unchanged).<sup>3</sup>

The 1906 Act covered all substances which were recognized or used as drugs at that time. Its wide coverage is apparent from its language:

all medicines and preparations recognized in the United States Pharmacopoeia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation or prevention of disease of either men or other animals.

Act of June 30, 1906, c. 3915 Section 6, 34 Stat. 769.

Under the second grandfather clause which is quoted above, a drug may escape the "new drug" machinery if it was marketed or officially recognized as a drug at any time before June 25, 1938, but after June 30, 1906. So if Laetrile was marketed or officially recognized as a cancer drug it would not have to be subjected to the instrumentalities which exist for new drugs under the 1962 Amendments even though it is not generally recognized as safe or effective.<sup>4</sup>

<sup>3</sup> See *Weinberger v. Hynson, Westcott and Dunning, Inc.*, 412 U.S. 609, 634, 93 S.Ct. 2469, 37 L.Ed.2d 207 (1973).

<sup>4</sup> We do not wish to convey that Laetrile could be marketed if it was found to be toxic or otherwise harmful, for even if Laetrile is not a "new drug" it is a drug subject to the prohibitions of Section 301 of the Act, 21 U.S.C. Section 331(a), and this provision makes unlawful "The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded." A drug is "misbranded" if "it is dangerous to health when used in the dosage, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof." Section 502(j) of the Act, 21 U.S.C. Section 352(j).

So, even though the drug is grandfathered it may still be excluded as dangerous to health. The difference between unsafe and dangerous is not great. It might be judged in accordance with scientific viewpoints as of different dates. Thus the Section 502(j) standard would look to the current assessments of safety.

Our reading of this second grandfather clause is in accord with the transitional provision of the 1962 Amendments, *supra*, which

## II.

## SUMMARY OF REMAINING QUESTIONS

From what we have said above there remain some questions to be determined. These are:

(1) Was Laetrile marketed on October 9, 1962, as a cancer drug and was it then generally recognized as "safe?"<sup>5</sup>

(2) Was Laetrile recognized or used as a cancer drug under the same conditions of present use during the period when the Food and Drugs Act of 1906 was in effect, June 30, 1906 to June 25, 1938?

If the answer to either of these is "yes," Laetrile would be exempt as a "new drug" under the Food, Drug and Cosmetic Act. We regard these questions as substantial, difficult and doubtful so as to support the granting of a preliminary injunction.

The FDA has argued that they have not issued any regulation or rule which specifically or positively forbids the administration of Laetrile. This is true. However, the FDA has made an administrative determination that Laetrile is a new drug and this places the plaintiff in a position in which he has to admit that it is a new drug in order to get the FDA to move. As a result he could not be heard to say that they have not effectively stymied the use of this drug. The FDA has

exempts from new drug status any drug "not a new drug as defined by section 201(p) of the basic Act then in force." P. Law 87-781, Section 107(c)(4)(B).

<sup>5</sup> The FDA argues that a drug offered for use in a life-threatening disease that is not "effective" is thereby not "safe" either. Thus even under the pre-1962 law Laetrile would have to satisfy effectiveness criteria. This argument may lose its force in the case of a terminally-ill patient or in the case of a patient suffering from a disease for which there are in fact no "effective" remedies. Compare *Duvoric v. Richardson*, 479 F.2d 242 (7th Cir.), cert. denied, 414 U.S. 944, 94 S.Ct. 232, 38 L.Ed.2d 168 (1973). See also *CIBA v. Weinberger*, 412 U.S. 640, 660 n.2, 93 S.Ct. 2495, 37 L.Ed.2d 230 (1973). In any case, this argument should be considered in the first instance in the further proceedings in this matter; the issue is not before us for resolution.

done this without citing any facts whatsoever, merely a conclusion, and this is the kind of declaratory order that was before the Court in *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 625-27, 93 S.Ct. 2469, 37 L.Ed.2d 207 (1973). There the Court upheld the FDA's power to declare that a substance is a "new drug" under the Act, but also held that an order of this kind is reviewable by a district court. 412 U.S. at 609, 93 S.Ct. 2469. In view of the dearth of evidence in support of the FDA's determination, it was entirely proper for the trial court to entertain this case.

From what has been said it is obvious that we are not in agreement with the trial court's opinion that the FDA has to approve or disapprove any new drug even in the absence of an application that satisfies the statutory mandate. As we have noted, Section 505(b) of the Act specifically requires the filing of a new application by the proponent of a new drug. The FDA simply rules on the application as submitted.<sup>6</sup> Congress in writing Section 505(b) was relying on the ability and willingness of the pharmaceutical companies to present new drugs. It follows that the FDA was not compelled to pursue this new drug procedure in the Laetrile situation in the absence of an application. See *Rutherford v. American Medical Ass'n*, 379 F.2d 641 (7th Cir. (1967), cert. denied, 389 U.S. 1043, 88 S.Ct. 787, 19 L.Ed.2d 835 (1968) (no FDA duty to initiate approval procedures for Krebiozen).

We are unable, however, to see how the FDA can escape the obligation of producing an administrative record

<sup>6</sup> See H.R. Rep. No. 2139, 75th Cong., 3d Sess. (April 14, 1938) at 9:

This provision (Section 505) will not put the Federal Government into the business of developing new drugs, nor will it require the Government to duplicate laboratory and clinical tests made by responsible manufacturers. The provision merely sets up a method for the authoritative review of the manufacturer's tests and will not unreasonably delay the introduction of new drugs in the market. It provides for court review of the decisions of the administrative agency adverse to the manufacturer.

See also H.R. Rep. No. 2464, 87th Cong., 2d Sess. (September 22, 1963) at 3.



to support its determination of the first and more fundamental issue that Laetrile is a *new* drug, for it is not a new drug merely because they say it is. Moreover, such a conclusory ruling precludes effective review under 5 U.S.C. Section 706(2). Cf. *Weinberger v. Hynson, Westcott & Dunning, Inc.*, *supra*, which holds the new drug decision by way of 5 U.S.C. Section 554(e) to be reviewable in a district court. To support its determination the FDA in the case at bar would have to present substantial evidence to support the proposition that Laetrile is not generally recognized among qualified experts as "safe and effective," and that Laetrile is not grandfathered by either of the exemptions discussed above.

It seems doubtful that the FDA has in fact developed an administrative record adequate under 5 U.S.C. Section 554(c) and hence there is probably nothing which is presently available for a court to review. Nothing in the record suggests that the FDA has dealt with Laetrile in a rule-making proceeding under Section 701 of the Act, 21 U.S.C. Section 371. Compare *National Nutritional Foods Ass'n v. Weinberger*, 512 F.2d 688 (2d Cir. 1975). Hence, if this is true the appropriate procedure for the district court is to remand the case back to the FDA for proceedings adequate to develop a record supportive of the agency's determination; the proceedings should give Laetrile proponents an opportunity to express their views. This is a result which is also supported by the Supreme Court decision in *Weinberger v. Bentex Pharmaceuticals*, 412 U.S. 645, 93 S.Ct. 2488, 37 L.Ed.2d 235 (1973). There the district court faced with a similar problem referred the matter to the FDA for initial determination. See 412 U.S. at 652-54, 93 S.Ct. 2488. The question whether the drug is to be recognized as "safe and effective" or was "grandfathered in" are "the kinds of issues peculiarly suited to initial determination by the FDA." *Id.* at 653, 93 S.Ct. at 2494.

It seems obvious that there cannot be a court review unless there is a decent record made. We see no need to consider the constitutional issues which were cited by the district court nor do we regard the convening of a three-judge court to be necessary. The district court's

injunction can continue in effect pursuant to 5 U.S.C. Section 705.

We conclude that the preliminary injunction granted by the district court in this case should be and the same is upheld. At the same time, the cause is remanded for further proceedings consistent with the views expressed herein.

McWILLIAMS, Circuit Judge (dissenting).

I respectfully dissent and would vacate the judgment and order of the trial court. The judgment and order of the trial court enjoined the Secretary and his representatives "from preventing the plaintiff Glen L. Rutherford from purchasing and moving in interstate commerce, and having for his own personal use, not for sale, barter or to be given away to any other person an amount not in excess of six-months' supply of Vitamin B17 or laetrile, . . . ." That, as I understand it, was the extent of the judgment and order here complained of. In my view such injunctive order was improvidently entered and on appeal should be vacated.

UNITED STATES DISTRICT COURT  
W.D. OKLAHOMA

No. CIV-75-0218-B

GLEN L. RUTHERFORD, ET AL., PLAINTIFFS

v.

UNITED STATES OF AMERICA, ET AL., DEFENDANTS

Jan. 4, 1977

MEMORANDUM OPINION AND ORDER

BOHANON, District Judge.

On December 30, 1976, this matter came on for pre-trial conference, the plaintiffs appearing by their attorneys Kenneth Coe and Burton J. Johnson, Oklahoma City, Okl., and the defendants appearing by William S. Price, Asst. U.S. Atty., Oklahoma City, Okl., and Jay H. Geller, Associate Chief Counsel, Food and Drug Div., Dept. of Health, Education and Welfare, Los Angeles, Cal.

The United States Court of Appeals for the Tenth Circuit in its Opinion filed October 12, 1976, in this case stated in part:

"We are unable . . . to see how the FDA can escape the obligation of producing an administrative record to support its determination of the first and more fundamental issue that Laetrile is a new drug, for it is not a new drug merely because they say it is. . . .

It seems doubtful that the FDA has in fact developed an administrative record adequate under 5 U.S.C. Section 554(c) and hence there is probably nothing which is presently available for a court to review. Nothing in the record suggests that the

FDA has dealt with Laetrile in a rule-making proceeding under Section 701 of the Act, 21 U.S.C. Section 371. . . . Hence, if this is true the appropriate procedure for the district court is to remand the case back to the FDA for proceedings adequate to develop a record supportive of the agency's determination; the proceedings should give Laetrile proponents an opportunity to express their views. This is a result which is also supported by the Supreme Court decision in *Weinberger v. Bentex Pharmaceuticals*, 412 U.S. 645, 93 S.Ct. 2488, 37 L.Ed.2d 235 (1973). There the district court faced with a similar problem referred the matter to the FDA for initial determination. See 412 U.S. at 652-54, 93 S.Ct. 2488. The question whether the drug is to be recognized as 'safe and effective' or was 'grandfathered in' are 'the kinds of issues peculiarly suited to initial determination by the FDA.' *Id.* at 653, 93 S.Ct. at 2494."

Subsequent to the Circuit Court's remand to this Court, counsel for the defendants admitted in open court that the FDA, in determining Laetrile \* to be a new drug, had failed to create an administrative record consonant with the procedures outlined in the Administrative Procedure Act or in accordance with the rule-making procedure outlined in the Food, Drug and Cosmetic Act at 21 U.S.C. § 371. In so doing the FDA has left little to be reviewed beyond its bare determination. Under such circumstances there would be much injustice in sustaining the FDA's unsupported conclusion while, on remand, it sought ex post facto to muster evidence in support of such conclusion.

Viewing the agency's description of Laetrile as a "new drug," from the standpoint of the judicial review standards outlined at 5 U.S.C. § 706, the Court would be compelled to find such determination to be "unsupported by substantial evidence," and to conclude that the agency

\* The Court finds from the record that Laetrile, Amygdalin and Vitamin B-17 are all one in the same, and the term Laetrile will be used to represent all three.

had failed to comply with its burden of proof in this matter.

In the above-quoted Opinion, the Circuit Court emphasizes that Laetrile is not to be considered a "new drug" under the law merely because the FDA has said so, but rather that said determination must be supported by substantial evidence. The statutory presumption in favor of administrative determinations is based on the premise that such determinations are presumed to be supported by substantial evidence until a reviewing court has determined otherwise. Such presumption was overcome when FDA counsel admitted that no competent administrative record had ever been developed in support of the agency's determination. As a matter of law then, such determination is not supported by substantial evidence and cannot be sustained. *Nickol v. United States*, 501 F.2d 1389 (10th Cir. 1974); *Heber Valley Milk Co. v. Butz*, 503 F.2d 96 (10th Cir. 1974); *Bailey v. Weinberger*, 380 F.Supp. 863 (D.C. Kan. 1974).

Having ascertained, during the December 30, 1976, hearing, that a competent administrative record did not exist, the Court then requested that the FDA make available to the Court the written basis for the agency's determination with regard to Laetrile, no matter how casual or unstructured its form or content might be; whereupon the Court was advised that no such rationale existed in any form. Clearly, federal agencies may not rule by fiat invoking only some unexplained application of their own expertise in defense of policy decisions they have made. *Chemical Leaman Tank Lines, Inc. v. United States*, 368 F.Supp. 925 (D.C. Del. 1973). Based on the complete absence of any evidence tending to establish a rational basis for the agency's determination, the Court would also be compelled to find, in applying the standards of 5 U.S.C. § 706, that the agency's determination was "arbitrary, capricious," and represented "an abuse of discretion," and that it should also be overturned for these additional reasons.

In consideration of the fact, however, that the lack of an administrative record precludes judicial review at this time in any meaningful sense, and in order to grant

both sides an opportunity to fully prepare and present their respective points of view, and consistent with the Circuit Court Opinion in this matter, the Court has determined that this case should be remanded to the FDA so that an administrative record can be constructed and a meaningful judicial review subsequently held. In view, however, of the complete absence of any good-faith agency record in support of its position in this case, as the record here is not merely incomplete, but virtually nonexistent; and in appreciation of the fact that depriving a terminally ill cancer patient of a substance he finds therapeutic, whether such benefit is physical or psychological, creates the very real risk that irreparable injury might be sustained.

IT IS HEREBY ORDERED, pursuant to 5 U.S.C. § 705, that while this case is on remand to the FDA, and until such time as the FDA proffers to the Court an administrative record containing substantial evidence in support of its determination that Laetrile is a "new drug" under the terms of the relevant statute, such determination is held to be without force or effect as to the plaintiff class in this case, and defendant FDA is hereby enjoined and restrained from preventing plaintiffs' importation or interstate transportation of Laetrile for purposes of their own consumption under the terms of the Food and Drug Act, including § 505(a) of the Act, 21 U.S.C. § 355(a).

IT IS FURTHER ORDERED that on remand an administrative record shall be developed within 120 days from the date hereof, and a copy of such record and administrative determinations resulting therefrom shall be filed with the Clerk of this Court and the plaintiffs within 30 days thereafter.

Such administrative hearing should be concerned with the issue of whether Laetrile is exempt from the "new drug" application requirements of the Food and Drug Act, § 505(b), 21 U.S.C. § 355(b), by virtue of the "grandfather" clauses, and also with the issue of whether Laetrile is "safe and effective," as set out in the Circuit Court Opinion.



The plaintiffs herein have moved this Court for an Order directing the FDA to hear testimony and evidence of Dr. Dean Burk, Washington, D.C., and Dr. Ernest Krebs, Jr., San Francisco, California, as experts in their field, and also evidence and testimony of Mike Culbert, Edward Griffin and Mike Spencer, as research historians. This Court is without authority to enter such an Order; however, the Court believes that the FDA might desire to invite these persons to participate in the administrative proceedings and to receive into evidence their views with reference to the history and safety and effectiveness of Laetrile.

Pursuant to the request of the plaintiffs and based upon the pleadings and evidence in this case, it is hereby determined that this suit meets the class action requirements of Rule 23, Federal Rules of Civil Procedure, and therefore,

IT IS FURTHER ORDERED that this suit shall be certified and hereafter treated as a class action.

UNITED STATES DISTRICT COURT  
W.D. OKLAHOMA

No. CIV-75-0218-B

GLEN L. RUTHERFORD, Individually and on behalf of a  
class composed of terminally ill cancer patients,  
PLAINTIFFS

v.

UNITED STATES OF AMERICA, ET AL., DEFENDANTS

April 8, 1977

MEMORANDUM OPINION

BOHANON, District Judge.

This cause came before the Court Friday, March 18, 1977, upon plaintiffs' "Application to Clarify Plaintiff Class" in the above-captioned class action. Plaintiffs requested that the Court enter Orders certifying the plaintiff class as including "all victims of cancer and their spouses who are responsible for the cost of treatment," and declaring as members of the plaintiff class all persons certified by a physician as having cancer. Defendants argued that plaintiff does not represent a class within the meaning of Rule 23 of the Federal Rules of Civil Procedure, that certification, in any event, should be limited to terminal cancer patients, that the FDA was within the scope of its authority in banning the importation and interstate transportation of laetrile, and that consequently the FDA should not be enjoined from preventing the use of laetrile.

Three basic issues emerge from the March 18, hearing and the evidence, arguments and submitted briefs.

*The Class Action Issue*

Plaintiffs seek class certification in terms detailed above. Defendants oppose certification, asserting "that

the class plaintiffs purport to represent is "too ill-defined and ephemeral in makeup" to render its members 'capable of definite identification,' and arguing that, at most, certification should encompass only terminal cancer patients.

The class action was an invention of equity, mothered by the practical necessity of providing a procedural device so that mere numbers would not disable large groups of individuals, united in interest, from enforcing their equitable rights. *Montgomery Ward & Co. v. Langer*, 168 F.2d 182, 187 (8th Cir. 1948). As a function of equity, it must be invoked and applied only in accordance with basic principles of fairness and reason. Under federal law, precepts of class action theory are delineated in Rule 23 of the Federal Rules of Civil Procedure.

Rule 23 possesses as its basic objectives the efficient resolution of the claims of many individuals in a single action, the elimination of repetitious litigation and possibly inconsistent adjudications involving requests for similar relief, and the establishment of an effective procedure for those whose economic position is such that it is unrealistic to expect them to seek to vindicate their rights in separate lawsuits. *Federal Practice and Procedure* § 1754, Wright and Miller.

Having carefully reviewed the facts and circumstances of this case, the applicable case law, and the requirements of Rule 23, the Court is persuaded it is appropriate to administer this matter as a class action.

In so deciding the Court has necessarily determined that plaintiff class is so numerous as to render joinder impracticable, that there are questions of law and fact common to the members of the class, that the claims of the representative plaintiffs are typical of the claims of the entire class, and that the representative plaintiffs will fairly and adequately protect the interests of the class. Additionally, the Court has concluded that defendants have acted on grounds generally applicable to the class in a way that renders injunctive relief proper. Rule 23, Federal Rules of Civil Procedure.

Although not specifically mentioned in Rule 23, an essential prerequisite of an action thereunder is that there must be a "class." *Weisman v. MCA, Inc.*, 45 F.R.D.

258 (D. Del. 1968). Whether a class exists is a fact question to be resolved in each case. *Clark v. Thompson*, 206 F.Supp. 539 (D. Miss. 1962). Rule 23 is to be construed liberally, and the class does not have to be so readily ascertainable that every potential member can be identified at the outset. *Carpenter v. Davis*, 424 F.2d 257 (5th Cir. 1970). Only the general outlines of the membership of the class must be determinable initially. *Berman v. Narragansett Racing Assn., Inc.*, 414 F.2d 311 (1st Cir. 1969). The requirement that there be a class will be deemed satisfied if class identification is sufficiently definite so that it is administratively feasible for the Court to determine whether a particular person is a member. See *Federal Practice and Procedure*, § 1760, Wright and Miller and cites therein.

Based on the evidence and arguments introduced since this case's inception, and to expedite administration of the Court's Order of January 4, 1977, plaintiff class is hereby certified as encompassing all "terminally ill cancer patients." The phrase "terminally ill cancer patient" refers to anyone who, in affidavit form as hereafter described, is declared by a practicing physician (M.D.) to be terminally ill.

Such affidavit shall include the following:

1. that there is histologic evidence of a rapidly progressive malignancy in the patient possessive of a high and predictable mortality rate; and
2. (a) that further orthodox treatment would not reasonably be expected to benefit the patient; or
  - (b) that laetrile will be administered only in conjunction with established and recognized forms of cancer treatment; or
  - (c) that the patient has made a knowing and intelligent election to take laetrile after being fully apprised of the full range of recognized treatments available and of the fact that laetrile is considered by most cancer experts to be of no value in combating the disease.

Defendants assert that early diagnosis and prompt treatment are critical in the management of cancer and that needless and untimely deaths will occur if laetrile is used in preference to established methods of cancer treatment. Such arguments have little applicability to that fraction of cancer patients whose lives orthodox medical science professes no capacity to preserve. To speak of laetrile as being "unsafe" for these people is bizarre. Additionally, it is connotative of a paternalism incompatible with this nation's philosophy as to the proper relationship between the government and the citizenry.

Rule 23 is designed to avoid a multiplicity of lawsuits while protecting the substantive rights of plaintiffs and defendants. *In Re Four Seasons Securities Laws Litigation*, 63 F.R.D. 422 (W.D. Okl. 1974). The salient issues in this case are such that defendants' position is in no way prejudiced by class action treatment; instead, defendants are saved the time and expense of defending a multitude of suits. At the same time, such treatment affords immeasurable benefits to the plaintiff class. Requiring litigation of protracted and expensive individual lawsuits would effectively serve to deny many terminal cancer patients the opportunity to have their claims adjudicated. Their disease has often left them with limited funds, and made time an even more precious commodity. It appears to the Court that ignoring the advantages of class action disposition of this case would evidence an indifference to judicial economy and the general spirit of the class action concept.

The question of whether to allow a suit to proceed as a class action is one primarily for the determination of the trial judge, and if he applies the correct criteria to the facts of the case, the decision should be considered to be within his discretion. *Gold Strike Stamp Company v. Christensen*, 436 F.2d 791 (10th Cir. 1970).

In cases such as this, where the ultimate effectiveness of a federal remedy may depend in large measure on the applicability of the class action device, all judicial discretion should be directed toward allowing the class action. *Esplin v. Hirschi*, 402 F.2d 94 (10th Cir. 1968).

Defendants urge that many cancer patients have no interest in the use of laetrile. The issue before this Court is not the wisdom of using Laetrile, but rather the right of cancer patients to do so if they choose. It is not fatal to the maintenance of a class action that some members of the class might prefer not to have violations of their rights remedied. *Leisner v. New York Telephone Company*, 358 F.Supp. 359, 372 (S.D. N.Y. 1973); *Norwalk Core v. Norwalk Redevelopment Agency*, 395 F.2d 920, 937 (2nd Cir. 1968). The rights of patients unimpressed by laetrile's alleged therapeutic qualities are in no way prejudiced by this decision. Such persons must be as free to disregard laetrile as are their fellows to invoke it.

Further consideration of the appropriate bounds of the certified class is possible since the Court always has the authority to change class designations should developments so require. *Guarantee Ins. Agcy. Co. v. Mid-Continental Rlty. Corp.*, 57 F.R.D. 555 (N.D. Ill. 1972); *Esplin v. Hirschi*, *supra* at 99.

#### *The Issue of Laetrile as a New Drug*

This Court makes no determination on the limited evidence before it as to laetrile's ability to combat the ravages of cancer. Defendants have introduced evidence tending to establish the general opposition of medical authority in this country to the use of laetrile. Contrarily, the Court is aware of instances of patients and physicians in various parts of the country emphasizing personal experiences with laetrile's ability to counter aspects of the disease's manifestations and discomforts. Regardless, such issue is not before the Court, and the Court is cognizant that it possesses "neither the facilities nor the expertise" to independently determine the drug's therapeutic value. *Tutoki v. Celebrezze*, 375 F.2d 105, 107 (7th Cir. 1967).

It is unlawful to introduce any "new drug" into interstate commerce previous to the FDA's approval of a "new drug application" (NDA) establishing such drug as "safe" and "effective" for its intended use. The FDA has banned the importation and interstate shipment of



laetrile on grounds that an NDA on its behalf has neither been filed nor approved.

In support of its position that plaintiffs are entitled to no substantive relief, defendants urge, *inter alia*, that the initial determination of the safety and efficacy of a "new drug" is the responsibility of the FDA, that FDA has no duty to approve a "new drug" in the absence of an NDA, and that the administrative procedures applicable to new drugs and outlined in the Federal Food, Drug and Cosmetic Act must be exhausted before a court has jurisdiction. These arguments are only relevant if the premise is accepted that laetrile is, in fact, a "new drug."

It is clearly established that FDA has power to determine whether a particular drug requires an approved NDA in order to be sold to the public. *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609, 624, 93 S.Ct. 2469, 37 L.Ed.2d 207 (1973). Its determination that a product is a "new drug" is, of course, reviewable. *Weinberger v. Hynson*, *supra*, at 627, 93 S.Ct. 2469. FDA does not have unbridled discretion to do what it pleases. Its procedures must satisfy the rudiments of fair play. *Weinberger v. Hynson*, *supra*. Where FDA declares a "new drug" where no NDA is in effect and no manufacturer is submitting an NDA, such declaration is reviewable by the district court under the Administrative Procedure Act, 5 U.S.C. § 701 et seq.; *Weinberger v. Hynson*, *supra*.

In an opinion in this same case, *Rutherford v. United States*, 542 F.2d 1137, 1143 (10th Cir. 1976), the Circuit Court held that FDA could not escape the obligation of producing an administrative record to support its determination that laetrile is a new drug, noting that "it is not a new drug merely because they [FDA] say it is." The Court further observed that based on the record in the case it appeared doubtful that FDA had in fact developed such an administrative record, and added that "to support its determination, FDA in the case at bar . . . would have to present *substantial evidence* to support the proposition that laetrile is not generally recognized among qualified experts as 'safe and effective' and

that laetrile is not grandfathered by either of the exemptions discussed above." (emphasis supplied)

As to the "grandfather clauses" the Circuit Court specifically found that if laetrile were either marketed as a cancer drug between 1938 and 1962 and recognized as safe, or if used as a cancer drug between 1906 and 1938 under the same conditions as presently used, it is exempt from being classified as a "new drug" by virtue of definitions contained in the Federal Food, Drug and Cosmetic Act. *Rutherford v. United States* (10th Cir.) *supra* at 1141.

Defendants recognize in their submitted brief that: "With respect to the grandfather clause of the 1962 amendments, the test generally is whether Laetrile was 'marketed before 1962 for exactly the same uses for which it is presently being sold and was generally recognized as safe for those uses.' *Tyler Pharmacal Distributors, Inc. v. United States Department of Health, Education and Welfare*, 408 F.2d 95, 99 (7th Cir. 1969)."

Nonetheless, FDA contends that if laetrile were marketed prior to 1962 it must still be shown to have been "effective" as well as "safe" if employed in the treatment of "a life-threatening disease."<sup>1</sup> *Durovic v. Richardson*, 479 F.2d 242 (7th Cir. 1973). The Supreme Court in *Weinberger v. Hynson*, *supra*, stated that "the 1962 amendments [of the Food, Drug and Cosmetic Act] for the first time gave FDA power to scrutinize and evaluate drugs for effectiveness as well as safety." 412 U.S. at 630, 93 S.Ct. at 2483. In any event, the case relied upon by FDA is clearly distinguishable from the case at bar. In *Durovic v. Richardson*, *supra*, the Court held that "(a)ny delay in the institution of effective therapy (e.g., radiation, surgery, effective chemotherapy) caused by the use of an ineffective drug allows the disease to pro-

<sup>1</sup> "The FDA argues that a drug offered for use in a life-threatening disease that is not 'effective' is thereby not 'safe' either. Thus even under the pre-1962 law Laetrile would have to satisfy effectiveness criteria. This argument may lose its force in the case of a terminally-ill patient or in the case of a patient suffering from a disease for which there are in fact no 'effective' remedies." *Rutherford v. United States* (10th Cir. 1976) *supra*, note 5 at 1142.

gress beyond control. Delay means almost certain death." Significantly, in the present case plaintiff class is comprised of persons already determined to be terminally ill. Adopting FDA's rationale would mean that an individual suffering from a life-threatening disease for which there exists no known effective treatment would not lawfully be entitled to any treatment at all since no drug could be deemed "generally recognized as effective" in such a situation.

Congress undoubtedly possesses the authority to proscribe drugs it considers dangerous to the public welfare. *Weinberger v. Hynson, supra* at 622, 93 S.Ct. 2469. The record in this case does not necessarily disclose any such Congressional intent as to laetrile. The FDA is not empowered to enforce its convictions concerning laetrile on the basis of its congressional mandate to monitor the introduction of "new drugs" into our society, if in fact laetrile has been used for decades in the treatment of cancer, and without ill effect. As implicitly recognized in *Rutherford v. United States*, (10th Cir. 1976) *supra*, the issue of the efficacy of laetrile is, at most, of secondary importance in this case. The legality of FDA's ban on laetrile is under attack on the theory that FDA arbitrarily and without sufficient basis in fact characterized laetrile as a "new drug;" so far FDA has presented little, if any, evidence to combat that allegation.

#### *The Issue of Injunctive Relief*

On August 14, 1975, this Court enjoined defendants from preventing the use of laetrile by the then named plaintiff in this action. Such injunction was subsequently upheld on appeal, the Circuit Court determining that the issues raised by FDA's classification of laetrile as a "new drug" were sufficiently "substantial, difficult and doubtful so as to support the granting of a preliminary injunction," and the case was remanded for further proceedings. *Rutherford v. United States*, (10th Cir. 1976), *supra*, at 1142. Thus the issue of this Court's jurisdiction to enter such an injunction has already been disposed of on appeal.

On January 4, 1977, this Court entered an Order remanding the case to FDA for development of a proper administrative record, and directing that "until such time as the FDA proffers to the Court an administrative record containing substantial evidence in support of its determination that laetrile is a 'new drug' under the terms of the relevant statute, such determination is held to be without force or effect as to the plaintiff class in this case, and defendant FDA is hereby enjoined and restrained from preventing plaintiff's importation or interstate transportation of laetrile for purposes of their own consumption under the terms of the Food and Drug Act, including § 505(a) of the Act, 21 U.S.C. § 355(a)."

Generally, if the questions presented in a suit for injunction are grave and difficult, and the injury to the moving party will be irreparable if the relief is denied, while the inconvenience and loss to the opposing party will be inconsiderable if the relief is obtained, the injunction should be granted. *Morton Salt Co. v. City of South Hutchinson*, 159 F.2d 897, 899 (10th Cir. 1947).

Plaintiff class is in danger of suffering irreparable injury if relief is postponed or denied. Any legal right they might possess to use laetrile may be of academic value if secured only at some undetermined future time. For the terminally ill the phrase "justice delayed is justice denied" contains special significance. Defendants' potential loss from the granting of injunctive relief is slight at most. Certainly defendants are charged with an important responsibility in safe-guarding the public from dangerous drugs, and they are to be commended for pursuing the task diligently. Nonetheless, the danger in the use of nontoxic but unproven cancer treatments by the public "is in their delaying or foregoing diagnosis and treatment which is generally recognized by the medical profession as beneficial and effective." *United States v. General Research Laboratories*, 397 F.Supp. 197, 199 (C.D. Calif. 1975). "Where a person is terminally ill with cancer and unresponsive to other treatments, the public harm is considerably reduced." *Carnohan v. United States*, Civ. No. 77-0010-GT (S.D. Calif. 1977).

In most instances in which relief in the form of a preliminary injunction is sought, the burden is upon the



movant to establish by clear proof that he will probably prevail when the merits are tried, and that irreparable injury will be suffered unless injunctive relief is granted. *Penn v. San Juan Hospital, Inc.*, 528 F.2d 1181, 1185 (10th Cir. 1975); *Crowther v. Seaborg*, 415 F.2d 437 (10th Cir. 1969); *Automated Marketing Systems, Inc. v. Martin*, 467 F.2d 1181 (10th Cir. 1972). Even under this more stringent standard, injunctive relief would still lie. The record in this case discloses many indications that laetrile may well be established to have been marketed for the last twenty years or more as a cancer treatment, to have been generally regarded by most experts as "safe," even if not "effective," and thus to be exempt from "new drug" classification by virtue of the previously discussed "grandfather clause" provision. Defendants' brief contains references to the report of the Cancer Commission of the California Medical Association published in 1953, which report on its face establishes the longevity of laetrile's recognized use. While concluding that laetrile was ineffectual as a "cure" for cancer, the report generally regarded it as safe and perhaps even palliative to some degree. Interestingly, the 1976 edition of the FDA Code Regulations (21 C.F.R. 121.101(e)(2)), as well as multiple earlier editions, places amygdalin<sup>2</sup> on the "Generally Recognized as Safe List."

#### Conclusion

Defendants adamantly urge that the use of laetrile is expensive, ineffectual and unjustifiable. Such contentions are serious and cannot be lightly regarded.

Of some significance, however, is the fact that laetrile's high cost is undoubtedly a direct consequence of its illegality in the United States; ironically, this requires travelling all the way to Mexico to enjoy its use lawfully.

This case raises questions of fundamental political and philosophical consequence. Freedom of choice neces-

<sup>2</sup> "The Court finds from the record that Laetrile, Amygdalin and Vitamin B-17 are all one in the same, and the term Laetrile will be used to represent all three." *Rutherford v. United States*, 424 F. Supp. 105 (W.D. Okla. 1977).

sarily includes freedom to make a wrong choice, and there is much force to the argument that matters of the type herein under discussion should be left ultimately to the discretion of the persons whose lives are directly involved.

The point can be couched in simple terms. Many intelligent and mentally competent citizens in this nation have made a deliberate decision that they would like to employ an unproven and largely unrespected treatment in an effort to comfort, if not save, lives that orthodoxy tells them have already been lost. They do so with an acute awareness of professional medicine's assessment of their choice. Their decision should be respected.

An appropriate Order will be entered herein.

#### ORDER AND DECREE

Based upon the Memorandum Opinion filed herein this day,

IT IS HEREBY ORDERED that plaintiff class in the above-captioned case is certified as encompassing all "terminally ill cancer patients." The phrase "terminally ill cancer patient" refers to anyone who, in affidavit form as hereafter described, is declared by a practicing physician (M.D.) to be terminally ill.

Such affidavit shall include the following:

1. that there is histologic evidence of a rapidly progressive malignancy in the patient possessive of a high and predictable mortality rate; and
2. (a) that further orthodox treatment would not reasonably be expected to benefit the patient; or
  - (b) that laetrile will be administered only in conjunction with established and recognized forms of cancer treatment; or
  - (c) that the patient has made a knowing and intelligent election to take laetrile after being fully apprised of the full range of recognized treatments available and of the fact that laetrile is considered by most cancer experts to be of no value in combating the disease.



IT IS ALSO HEREBY ORDERED that the defendants in this action, the United States of America, its agents, agencies and instrumentalities, including, in their official capacities, Joseph A. Califano, Secretary of Health, Education and Welfare, Donald Kennedy, Commissioner of the Food and Drug Administration, and Vernon D. Acree, Commissioner of U.S. Customs Service, and their successors and agents are enjoined from impeding or preventing the importation and interstate transportation of laetrile by any members of the plaintiff class or their duly designated agents.

IT IS FURTHER ORDERED that such laetrile can be imported and utilized solely for the personal use and benefit of the plaintiff class members.

The Clerk shall send, by registered mail, a certified copy of this Order and Decree to each department administrator referred to herein.

## STATEMENT CONCERNING LAETRILE

by

Frank J. Rauscher, Jr., Ph.D.  
Director, National Cancer Program  
National Cancer Institute

The National Cancer Institute, under the leadership of several Directors, has been deeply concerned with the Laetrile issue. During my tenure as Director, the issue has become a full-fledged public health problem which now, in my estimate, poses a real hazard to cancer patients.

Laetrile is touted by its advocates as a substance which may offer objective and subjective benefits to cancer patients. The basis for such claims is very poorly defined. Perhaps the main offering point, transmitted through extra-scientific channels, is that Laetrile is completely non-toxic and thus can be administered without hazard to patients. The idea of a patient's freedom of choice in selecting therapies is also frequently expressed.

The strength of such appeals is not difficult to understand. Cancer, a group of more than 100 quite different clinical entities, afflicts through death and disability many thousands of individuals yearly. There are few individuals or families who have not been affected directly or indirectly by the occurrence of cancer. There is probably no disease that is feared more or, in spite of the efforts of the work of organizations such as NCI and the American Cancer Society, more poorly understood. Thus, the cancer patient is understandably receptive to the idea that a complex problem can lend itself to a simple solution, in other words, that the disease can be controlled without the discomfort and risk of any non-toxic agent if it cannot be expected to produce objective clinical benefit.

The argument may be made that cancer patients who have failed to respond to other therapies should be allowed to receive Laetrile. The problem with that idea is that the line cannot be so finely drawn. If the drug

The idea that patients should be allowed to freely select their treatments is, in my mind, a snare and a delusion. In dealing with any medical problem and particularly a dread disease such as cancer, the patient should be able to have the information necessary to select a well-qualified physician who can assure the patient that the best of available diagnostic and therapeutic methods will be applied in the best available facilities. He should have assurance that the properties of the drugs he receives have been well defined. These are complex matters that can be assured only through the effective functioning of complex societal processes, which include medical training and licensure, medical research and careful formal evaluation and regulation of the availability of materials, methods and facilities. These processes may at times be slow and cumbersome but without them there would be little assurance of any quality and effectiveness in medical care. The patient would be fair game for the callous or well-intended advocate of methods that might be ineffective if not harmful.

Food and Drug Administration

Docket No. 77N-0048

IN THE MATTER OF

## A RULEMAKING PROCEEDING CONCERNING LAETRILE

AFFIDAVIT OF ROBERT S. K. YOUNG, M.D., Ph.D.

COUNTY OF MONTGOMERY )  
 ) SS  
STATE OF MARYLAND )

Before me personally appeared Robert S. K. Young, M.D., Ph.D., who first being duly sworn, deposes and says:

1. I am a physician licensed to practice in the States of Maryland and New York. I received an M.D. Degree from Yale University in 1970. I was an intern at the Mt. Sinai Hospital, New York, New York in 1971.
2. I was an assistant resident in internal medicine at the Mt. Sinai Hospital, New York, New York in 1972.
3. I was a fellow in medical oncology at the National Cancer Institute, National Institutes of Health, Bethesda, Maryland in 1973 and 1974.
4. I am a pharmacologist. I received my Ph.D. from Yale University in 1969.
5. Since 1975, I have been adjunct assistant professor of pharmacology at Georgetown University Schools of Medicine and Dentistry. Since 1975, I have been an instructor of pharmacology in the graduate program, Foundation for Advanced Education in the Sciences, National Institutes of Health, Bethesda, Maryland. My curriculum vitae is attached hereto as Exhibit A.
6. I am Group Leader for the oncologic drug class, Bureau of Drugs, Foods, Food and Drug Administration, Rockville, Maryland.

7. My professional duties require that I be conversant with the scientific literature and methodology in the field of cancer chemotherapy, both therapeutic and experimental, clinical and preclinical, and I am familiar with radiation therapy for cancer.

8. Under Section 107(c)(4) of P.L. 87-781, the 1962 Amendments to the Federal Food, Drug, and Cosmetic Act, Laetrile would not be considered a "New Drug" subject to the requirements of an approved New Drug Application under 21 U.S.C. 355, if each of the following conditions are met:

- (a) On October 9, 1962, Laetrile was not a new drug as defined by Section 201(p) of the basic Act as then in force (21 U.S.C. 321(p));
- (b) On October 9, 1962, Laetrile was commercially used or sold in the United States;
- (c) On October 9, 1962, Laetrile was not covered by an effective (new drug) application under section 505 of the basic Act then in force (21 U.S.C. 355);
- (d) Laetrile, as used on October 9, 1962, was the identical drug entity it presently is and
- (e) The labeling for Laetrile represents it as being intended solely for use under conditions prescribed, recommended, or suggested in its labeling on October 9, 1962.

In the event that Laetrile does not meet each and every one of these conditions, it is not entitled to the Section 107(c)(4) grandfather exemption from the new drug provisions of the Federal Food, Drug, and Cosmetic Act. Laetrile is not entitled to exemption under this grandfather clause because of numerous changes which have occurred in the composition, labeling, routes of administration, dosage form, intended uses, and identity of the drug substance. Some of these many changes are described and discussed below.

9. I have reviewed and compared labeling and other information contained in the New Drug Application for

Laetrile (NDA 14-032) which the Food and Drug Administration received on October 3, 1962, with labeling for the drug obtained by FDA during an establishment inspection of Krebs Laboratories of San Francisco, California. Exhibit 'B' attached hereto contains excerpts from the New Drug Application which I have reviewed. Exhibit 'C' includes the labeling obtained during the April 23, 1965 inspection.

10. I find that the 1965 labeling is significantly different from that in the 1962 New Drug Application. Among the differences that I noticed are:

- (a) The formulation of the drug had been changed. In 1962, the formulation contained N, N diisopropylammonium iodide and saccharides in addition to amygdalin and these materials were to be reconstituted with an isotonic solution. In 1965, the formulation contained only amygdalin and this material was to be reconstituted with water, which is not isotonic.
- (b) The class of patients for whom the drug is recommended had been changed. In 1962, the label characterizes the drug as a palliative agent for use in "cancers beyond aid by standard agents," and warns that *"It is not to be employed to the exclusion of surgery, radiation or similar standard modalities so long as they are indicated."* The 1965 labeling states that "Laetrile does not palliate, it acts chemically to kill the cancer cell selectively without injury to the normal tissues of the body." It goes on to warn that "The physician who is using laetrile to palliate his patients is not doing justice to his patient."
- (c) The interaction of Laetrile with other forms of cancer treatment had been changed. In 1962, the label states Laetrile "has no known therapeutic incompatibilities." It goes on to warn that "the general enhancement of the clinical condition of the patient is not to be considered as justification for the exclusion of standard modalities so long as they are applicable." In



the 1965 material, the directions state that "The less drugs and medicines given, during the Laetrile treatment, the better. What should be especially avoided is . . . other cancer therapies, strong drugs . . . etc."

- (d) The recommended route of administration had changed. In the 1962 labeling, "intravenous administration is preferred." The 1965 labeling advises that "Whenever it's possible to administer Laetrile by injection into the artery supplying the involved area this administration should be used." Specifically, injection into the external carotid or its branches, abdominal aorta, or internal iliac arteries is recommended. The 1965 labeling also recommends injection into the vault of the vagina and scrotal sac, and rectal enemas. I am generally familiar with the literature and reports relating to Laetrile and am aware that since 1965, there has been commercial distribution of dosage forms of Laetrile including tablets containing Amygdalin, capsules of ground defatted apricot kernels, and a milkshake mix containing Amygdalin all intended for oral use.
- (e) The claimed mechanism of action of the drug had changed. In the 1962 material, the "Beardian thesis" was discussed as a theory. The 1962 labeling made no claim that Laetrile is a vitamin or provitamin, or that cancer is a deficiency disease. The 1965 labeling states that "Cancer is a deficiency disease" and there is a presentation of what role amygdalin plays in the therapy of cancer in light of cancer as deficiency disease.

11. All of the above changes are medically important or have medically important implications that must be reviewed scientifically. In the same order as I have reviewed them in 10, they are:

- (a) Formulation changes may reflect changes in the drug substance, and always reflect changes in the material to be administered.

Whenever the material to be administered is changed, it is important that the new material be essentially identical to the old material in strength, quality and purity.

- (b) The 1962 labeling restricts the use of Laetrile to those patients who all have had conventional therapy, and prescribes use for the purpose of palliation of their disease. The 1965 labeling states that this drug should be used to mitigate the effects of the disease and implies that the drug is of curative value. Since Laetrile has no demonstrable effect on cancer, to use Laetrile in lieu of conventional therapy is to condemn to certain death those patients with curable forms of cancer, and to prolong the pain and suffering of those patients with treatable forms of cancer.
- (c) The 1962 labeling warns that conventional therapy not be withheld during Laetrile administration. The 1965 labeling suggests a harmful interaction between Laetrile and conventional therapy. Again, since Laetrile has no demonstrable effect on cancer, to use Laetrile in lieu of conventional therapy is to condemn to certain death those patients with curable forms of cancer and to prolong the pain and suffering of those patients with treatable forms of cancer.
- (d) Changes in the route of administration of a drug must always be scientifically validated. A drug may not be effective or may be more toxic when given by different routes of administration. The recommendation in 1965 that the drug be given by intra-arterial injection is particularly hazardous. These high pressure blood vessels are difficult to enter successfully and are prone to continue bleeding after entry with a needle.
- (e) The claimed mechanism of action strongly suggest that Laetrile has a rational basis as a can-

cer therapy. Since it has no demonstrable value as a cancer therapy, to suggest that it has may influence some to use it who might not otherwise use it.

12. Discussion of whether the 1962 or 1965 labeling is more accurate or provides safe directions for use of Laetrile is pointless, since the drug is without demonstrable anticancer activity, and is inherently unsafe for use in humans. Because of these changes in Laetrile's labeling alone, it is in no event entitled to the grandfather exemption contained in Section 107(c)(4) of P.L. 87-781.

/s/ Robert S. K. Young, M.D., Ph.D.  
ROBERT S. K. YOUNG, M.D., Ph.D.

Subscribed and sworn to by the said Robert S. K. Young, M.D., Ph.D., before me this 25th day of March, 1977.

/s/ Mary B. Garrett  
Notary Public  
My Commission Expires:  
July 1, 1978

Dean Burk, March 25, 1977

re FDA Docket No. 77N-0048

DEAN BURK FOUNDATION, INC.  
4719 Forty-Fourth Street • Washington, D.C. 20016  
Telephone (202) 363-6279

*Deposition*

TO WHOM IT MAY CONCERN, and in particular, Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, Md. 20857, and Tenny P. Neprud, Compliance Regulation Policy Staff, same address.

I am DEAN BURK, President, Dean Burk Foundation, Inc., 4719 44th Street, Washington D.C., and under notaried [sic] oath depose and say, in the following pages (1-7) and attached Exhibits (A-M, 150 pp.), total 157 pp.

(1) I graduated from the University of California at Berkeley in 1923, and received my Ph.D. from that Institution in 1927. This Ph.D. was in the field of biochemistry, in the Department of Plant Nutrition, with a minor in chemistry in the Department of Chemistry.

(2) Prior to my forty-five years employment with the United States Government as a research civil servant (1929 to 1974), I did biochemical and nutritional work at the University of London (University College), Kaiser Wilhelm Institute for Biology in Berlin, Germany, and in the Department of General Physiology at Harvard University (1927 to 1929). I was associated with Cornell University Medical College, New York City, as Associate Professor of Biochemistry from 1939 to 1941.

(3) During my forty-five years of Civil Service with the United States Government, I worked in the Department of Agriculture from 1929 to 1939, and then in the National Cancer Institute of the National Institutes of Health of the Department of Health, Education and Welfare for thirty-five years (1939 to 1974). My last position with HEW before mandatory age-retirement in

1974, was that of Head of the Cytochemistry Section of the National Cancer Institute. I was Guest Scientist at the United States Naval Medical Research Institute, Department of Experimental Medicine, in Bethesda, Maryland from 1974 to 1976.

(4) Attached in Exhibit A, pp. 22-23, is a brief statement of my curriculum vitae listing various awards and appointments in my lifetime to date. I am listed in Who's Who in America and in Who's Who in the World. Approximately 60,000 Americans are listed in the Marquis Who's Who in America; only about 6,000 of these are listed in the Marquis Who's Who in the World, and I am one of them.

(5) I have been active in the field of cancer since 1927, now fifty years, and, in collaboration with several hundreds of scientists and medical doctors, have worked in nearly every field of cancer, and have produced over one hundred and fifty scientific papers in this field alone, out of a total of some 300 scientific papers altogether. Some of this work involved some five years of scientific study in Germany, and some three years of scientific work in England, together with other work and attendance at many international scientific congresses in still other European countries. I have performed tens of thousands of experiments with laetrile.

In the following pages and exhibits I shall attempt to show that, in my opinion, laetrile is generally recognized by qualified experts as a safe and effective treatment for cancer, as a food and vitamin, but not as a "new drug."

In attempting to arrive at a satisfactory distinction between a food and/or vitamin on the one hand, and a new drug on the other, the following considerations must be kept in mind:

(6) Although the Federal Food, Drug, and Cosmetic Act defines in Chapter II—DEFINITIONS—Sec. 201 (321) (g) (1) "The term "drug" means (A) articles recognized in the official United States Pharmacopeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis,

cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; . . ." nevertheless, foods and vitamins have been widely recognized as exceptions with respect to (A), (B), and (C) (cf. Exhibit A, pp. 4-7).

Thus, in a 15-page letter written on March 1, 1974 by then-FDA Commissioner Alexander M. Schmidt, M.D., to Arthur Koch, National Health Federation, 121 2nd Street, N.E., Washington, D.C. 20002, who had petitioned that fluoride be classified as a drug under the above-cited section of the F.D.C. Act, Commissioner Schmidt denied this petition, stating that

"The petition erroneously concludes that fluoridated water is a drug under the Federal Food, Drug, and Cosmetic Act. It is instead a nutrient, necessary in *normal diets to assure good health*, and is therefore *properly regulated as a food*."

"The petition misinterprets the definition of "drug" in the Federal, Food, Drug, and Cosmetic Act because it fails to distinguish between *nutritional (food)* and *therapeutic (drug)* uses of a substance. The petition argues that because the intended use of fluoridated water is aiding in the prevention of a disease, tooth decay, the substance is therefore a drug within the meaning of 21 U.S.C. 321 (pp. 5-9). This proposed interpretation of the statute is inconsistent with the design of the Act, however, and *cannot be sustained*."

"It is clear that a nutrient, offered as such, was not meant to be treated like a drug under the Act. The interpretation sought to be applied would result in *all food being treated as drugs*. That consequence would follow because the fundamental reason all food is eaten is *to prevent the appearance of diseases that result from improper diet*. Failure to eat enough food results in protein-calorie malnutrition diseases such as kwashiorkor and marasmus. Failure to take in all the proper nutrients results in *vitamin-deficiency diseases like scurvy and pellagra or in other abnormalities*."



"Underlying this concern for good nutrition is, of course, the intention to prevent disease. . . . General nutritional education does not constitute the specific claims for disease prevention that must accompany a product to make it a drug within the meaning of 21 U.S.C. 321 (g) (1) (B)." . . . "scientific and medical knowledge must be used to *distinguish nutritional from therapeutic uses of a substance.*" (Emphasing italics added).

(7) as a *vitamin* (B-17), amygdalin would be precluded from being classed as a new drug, in view of Congressional Law 94-278 (Proxmire Amendment) signed by the President April 22, 1976, and indeed also by the United States Court of Appeals, 2nd Circuit, decision of August 15, 1974 as upheld by the U.S. Supreme Court by virtue of denial of certiorari. (cf. Exhibit A, pp. 5-10).

Clearly, amygdalin acting as a food and vitamin, and playing a nutrition role in its mechanism of alleviation of human cancer, requires no designation as a new drug, any more than does vitamin C (ascorbic acid) in its mechanism of alleviation of scurvy, and similarly through the list of all other vitamins, as well as nearly all foods.

Let us now examine how the foregoing general considerations of (6) and (7) do in fact apply to the case of laetrile in particular, as a food and as a *vitamin*, and not a new drug.

(8) In the decision of the United States Court of Appeals, 10th Circuit (75-1725), the opinion is given that "As we view it, the reason that the Food and Drug Administration is anxious to classify Laetrile as a new drug is so as to bring it within the new drug certifications procedures of the Food, Drug and Cosmetics Act. Section 505(a) of the Act, 21 U.S.C. Section 355(a). This provision bars the introduction into interstate commerce of a new drug without an approved new drug application having been filed pursuant to the Act just cited." But, "the FDA's record is grossly inadequate and consists merely of a conclusory affidavit of an official of the FDA which in effect declares it (laetrile) *is a new drug because the FDA says it is* and thus is subject to all of the statutory vagaries of such a designation." (October 12, 1976).

Subsequently, upon remand to the United States District Court for the Western District of Oklahoma, Judge Bohanon in a Jan. 4, 1977 MEMORANDUM OPINION AND ORDER ordered that "pursuant to 5 U.S.C. Paragraph 705, that while this case is on remand to the FDA, and until such time as the FDA proffers to the Court an administrative record containing substantial evidence of its determination that Laetrile is a "new drug" under the terms of the relevant statute, *such determination is held to be without force or effect* as to the plaintiff class in this case," and that hereafter "this suit shall be certified and treated as a class action suit," under Rule 23 of the Federal Rules of Civil Procedure. Further, the Court stated, "Based on the complete absence of any evidence tending to establish a rational basis for the agency's determination, the Court would also be compelled to find, in applying the standards of 5 U.S.C. Paragraph 706, that the agency's determination was arbitrary, capricious," and represented "an abuse of discretion," and that it should be overturned for these additional reasons.

(9) To the judiciary considerations briefly outlined in (8), I may add that, in my judgment and experience, the FDA determination is scientifically without substantial basis, arbitrary, capricious, merely conclusory without evidence, and, I affirm, prevaricative, to an unbelievable degree, as indicated below. FDA officials and FDA outside appointees have made innumerable statements to the effect that laetrile is not a vitamin, but always, to my knowledge, in merely conclusory manner with clear and intended *neglect of overwhelming evidence to the contrary*, some of which I shall present in attached Exhibits for any and all to see and study. To paraphrase the wording of the 10th Circuit Federal Appellate Court, "because the FDA conclusorily declares that laetrile is not a vitamin (B-17) does not make it not a vitamin." As pointed out in (7) above, the status of laetrile as a vitamin (B-17), to be indicated below, proscribes and makes moot its being a new drug.

#### *Laetrile as Vitamin*

(10) To begin with, all vitamins are by Federal statute definition foods (cf. Exhibit A, pp. 1-2, 5-10); and,

as indicated in Exhibit B, laetrile is listed \* in the HEW-FDA GRAS List (foods "*Generally Regarded as Safe*") under the heading of natural extractive from bitter almond, apricot, or peach kernels (syn. seeds, nuts). The only specified proviso is that such extractive be "free from prussic acid." Exhibit C summarizes evidence that laetrile contains no ordinarily measurable or measured quantity of prussic acid, any and all statements to the contrary notwithstanding. Being on the GRAS List proscribes laetrile from being classified as a food *additive*, in accord with the Federal statute definition in the Federal Food, Drug, and Cosmetic Act—Chapter II, Definitions—Sec. 201(321)(s).

(11) To continue, pp. 18-21 of Exhibit A, summarizes the extensive evidence that has existed for over one hundred years, that laetrile, at conventionally applied dosages for cancer treatment is nontoxic in animals and man over a very wide range of application.

(12) Pp. 7-9 of Exhibit A gives a widely accepted definition of vitamins and their varying natures, background, and interpretation. The summarized definition at the top of p. 8 is in close harmony with that given by Professor David M. Greenberg, Emeritus University of California Medical School, and Consultant, Cancer Advisory Council, California State Department of Health, on p. 346 of his article in *Western Journal of Medicine*, vol. 122, May 1975, but Professor Greenberg makes in this article a studied neglect of his definition to the instance of laetrile data of the vitaminic nature of laetrile now to be reported, briefly summarized on p. 15 of Exhibit A, following discussion on pp. 11-14.

#### *Animal data.*

(13) p. 15 of exhibit A summarizes amygdalin efficacy against cancer in animals as observed in three widely separated countries of the world, and five laboratories therein, up to date of 1975; more such work has appeared since. Not all such data can be presented here—

\* P. 372 of the 1976 edition of FDA Code Regulations, Title 21 CFR 121.101(o)(2), and earlier editions.

by any means—but it may be illustrated in Exhibits D, E, and F as follow.

Exhibit D sets forth some of the data referred to in Item (1), p. 15, Exhibit A, taken by Dr. Kanematsu Sugiura, Sloan Kettering Cancer Center (New York).

Exhibit E sets forth some of the data referred to in Item (2), p. 15, Exhibit A, taken by the Southern Research Institute (Birmingham, Alabama) for the National Cancer Institute, concluding with statistical confirmations by others than myself.

Exhibit F sets forth a small fraction of the data taken by the Scind Laboratories (San Francisco), 1968.

In (13) above and (14) below, laetrile shows all the essential properties and attributes that define a *vitamin*, (cf. Exhibit A, p. 8, and p. 11; and Greenberg, J. West. Med. 122, p. 346, 1975) and, in this instance, a B vitamin: it is virtually nontoxic, water-soluble, an exogenous nutrient or food factor, and active in relatively small, essentially catalytic, non-calorific amounts, and is essential or beneficial in normal metabolism and/or physiologic functioning to *overcome deficiency lesions and symptoms of nutritional disease*. In the foregoing animal data the deficiency lesions and symptoms of nutritional disease are best illustrated by the action of amygdalin in lengthening of animal lifetime or decreasing development of metastases, or both, and increase in health and well-being, all properties objectively measured in the experiments reported, as may readily be seen upon detailed examination of the data.

#### *Human data.*

(14) Some of the first, clear-cut published data indicating a positive and vitamin action in humans was reported by the Cancer Commission of the California Medical Association in 1953 (*California Medicine*, 78, 320-326) and later republished by the California State Department of Health Cancer Advisory Board in 1963 et seq., which reported in a study of 44 terminal cancer patients that "all of the physicians whose patients were reviewed spoke of increase in the sense of well being and appetite, gain in weight, and decrease in pain (cf. Exhibit A,



bottom of p. 11 et seq.). Although the Commission regarded all of these criteria of action as being only subjective (an aspect not essentially material to definition of a vitamin), nevertheless all of these criteria are in principle objective also, as "perceptible to persons other than the patient" (dictionary definition of (objective")). [sic] The Commission also acknowledged a probable effect on nitrogen metabolism.

Since 1953, and to some extent before, scores of publications throughout the world have reported thousands of patients who appear from observing physicians' reports to have benefitted objectively as well as subjectively from administration of laetrile. It is idle to declare that such observations are totally without value, medically or scientifically, even if they do not represent ideal methods of ascertaining probable cause and effect relationship, which is, indeed, seldom if ever attained in the field of human cancer, any and all statements to the contrary notwithstanding. In any event, widely varying opinions on this aspect prevail in the field of medicine, to such an extent that no one opinion can as yet be said to be definitive and universally accepted, and probably never will be. In forthcoming weeks a book will appear by Dr. John Richardson, M.D. on his experiences with some 5000 cancer patients receiving laetrile along with related treatments, and somewhat later on a similar report by Dr. Ernesto Contreras is scheduled based on about the same number of patients. And, during the past year the Governments of Australia and Israel have set up clinical testing of laetrile on human cancer patients, based upon inspection visits by respective government medical appointees to study results and clinics of Drs. Richardson and Contreras and other medical centers in the United States and elsewhere, which Australian-Israeli testing would not have been set up without solid basis, results of which must be awaited.

Exhibit G reports laetrile clinical experiences of the leading German laetrile specialist, Dr. Hans Nieper, Hannover, Germany, from early 1971 to 1977. It is to be noted from the letter that most laetrile medical specialists do not use or recommend exclusive treatment by lae-

trile but in a setting of metabolic therapies, in all of which laetrile is regarded as vitamin (B-17), which, as in most vitamin regimens involves usually interrelated treatment with a number of other vitamins, since the action of a vitamin does not take place in a vacuum, but in a proper reasonable balance of other vitamins and indeed other foods.

In all or nearly all of the Legislature Hearings on the Alaska type laetrile bills (cf. Exhibit M) so far held in Maryland, Nevada, Washington, Arizona, Indiana, and South Dakota, patients testified personally who had undergone various forms of laetrile treatment after it had become evident that conventionally approved therapies were failing of successful result, and who were now surpassing the M.D.-predicted probable survival times, and many of them presented documented histories of their earlier and more recent statuses, from which it appeared that laetrile was having benefit. Again, ideal cause and effect relationships were not sought with laetrile any more than with conventional chemotherapeutic treatments. Petition campaigns to introduce "Alaska-type" bills are now underway in Florida, Hawaii, Texas, Ohio, Wisconsin, Louisiana, Massachusetts, Michigan, New Jersey, New York, North Carolina, Oklahoma, Kansas, Iowa, Illinois, and will almost certainly involve patients and documentation of the type just described in the already active Legislatures, where in the Committee Hearings and votings by one house or the other, the voting in favor of an "Alaska-type" bill has been overwhelming or nearly so, with failure in but one state, North Dakota.

Exhibit H presents a history of the initial representation of laetrile as a vitamin (B-17), involving human epidemiological considerations as well as animal indications, and Exhibit I briefly presents a recent summary of some current aspects. Exhibit J gives some indication of the extent of laetrile availability in the United States, some 1500 kg. of which are consumed per month by some 50,000 Americans. At least 200 kg. per month are manufactured in the United States. As indicated earlier, the 10th Federal Circuit has enjoined the FDA provisionally from preventing interstate commerce restrictions of dis-



tribution, etc., on the basis that the FDA must first produce evidence (administrative record) to justify any classification of laetrile as a New Drug; meanwhile laetrile remains simply a food by Federal Statutory definition, legally available in the United States as a food, and subject only to FDA Food (not New Drug) regulations, which are far less stringent.

As a vitamin (a class of food), laetrile cannot be classed by the FDA as a New Drug (or food additive), in any event, as indicated in (7) above. At the same time, this would render the question of "grandfathering" laetrile as a New Drug as now moot and superfluous. Exhibits K and L may be of interest in this connection, however, as they concern the use of laetrile in the treatment of cancer before 1962 and 1938 in the United States (cf. (8) above), i.e., before passage of the Kefauver and Copeland Amendments to the Federal Food, Drug, and Cosmetic Act.

Respectfully submitted as verified copy, in quadruplicate,

/s/ Dean Burk  
DEAN BURK,  
President, Dean Burk Foundation, Inc.  
National Cancer Institute, 1939-1974, Ret.

Subscribed and sworn to before me this 25th day of March, 1977.

/s/ [Illegible]  
Notary Public  
My Commission Expires:  
Dec. 11, 1977

## EXHIBIT I

## Deposition

## TO WHOM IT MAY CONCERN:

My name is Raymond Ewell of 56 Highgate Ave., Buffalo, New York. I hold a Ph.D. degree in chemistry from Princeton University and other degrees from Purdue University, George Washington University and the University of Toledo. From 1957 to 1973 I was vice-president for research, professor of chemistry and professor of chemical engineering at the State University of New York at Buffalo. Also, I lectured in a course in human nutrition in the Department of Biology. I retired in 1973 and since then I have worked part-time for the United Nations on problems of agriculture.

The first statement I want to make is that all the available facts indicate that *amygdalin* is essentially non-toxic to laboratory animals and to humans. Anyone who claims that amygdalin is a toxic substance is indulging in sophistry or pseudo-science or has never examined the facts. Amygdalin does have a very low toxicity, comparable to many foods such as salt, sugar, spices, condiments (e.g. MSG), and even some fruits and vegetables. All foreign substances have some toxicity in the animal organism, but many substances have very low toxicity and are therefore classified as GRAS (Generally Recognized As Safe). *Amygdalin* has never been classified as GRAS or not as GRAS primarily because only a few people consume *amygdalin* in its pure form either as a food supplement or as a flavoring agent. However, many people in many parts of the world consume substantial amounts of amygdalin as a component of almonds, fruit seeds, buckwheat, tapioca, lima beans and many other foods. The candy called "Marzipan" is especially rich in amygdalin reportedly as high as 20% amygdalin.

*Amygdalin* is a well-known organic chemical compound with the overall formula  $C_{20}H_{27}O_{11}N$ . It is called amygdalin because it was first isolated from almonds and identified by German chemists in 1830 (amygdalo is the

Greek word for almond). Correct chemical names for amygdalin are mandelonitrile diglucoside or mandelonitrile gentiobioside. Amygdalin is also known popularly as laetrile or Vitamin B-17. Pure amygdalin is manufactured by several reputable biochemical firms in West Germany, Switzerland, Italy, Monaco and Mexico. Amygdalin is made by alcohol extraction of apricot kernels or almonds followed by crystallization from the alcohol solution. Amygdalin has recently been approved by the Govern-[sic]

*Amygdalin* is a definite molecular compound comprising one benzaldehyde unit, one cyanide unit and two glucose units, firmly bound together in a molecule. Saying that amygdalin is toxic because it contains cyanide is like saying that common salt is toxic because it contains chlorine, which is a poison. However, we know that salt is only slightly toxic, even though large quantities of salt can be toxic to animals or humans (but not because it contains chlorine).

Moreover, a number of normal components of the human body contain cyanide. For example, Vitamin B-12 is essential to human health, and the Vitamin B-12 molecule contains cyanide in the same way that amygdalin contains cyanide.

I have had no first-hand experience in toxicity studies on *amygdalin*, but I have read reports from the Sloan-Kettering Institute (New York), Southern Research Institute (Birmingham, Alabama), Scind Laboratories (San Francisco) and laboratories in France, West Germany and Switzerland giving test results on animals showing that amygdalin is essentially non-toxic. One of these reports (I believe it was the Sloan-Kettering Institute) stated that the first slight indication of toxicity was noted in animal tests corresponding to 75 grams (3 ounces) of amygdalin per day for a 165 lb. man. Significant toxicity was noted at 150 grams (6 ounces) of amygdalin per day for a 165 lb. man. Many GRAS substances are toxic at these high levels. Most people who use amygdalin as a food supplement consume less than one gram per day, and even in cases where doctors have recommended intakes of 2 to 5 grams per day of amygda-

lin, no toxicity has ever been noted. Even 5 grams per day is only 1/15 of the level of 75 grams per day where Sloan-Kettering Institute noted the first slight indication of toxicity.

The California State Department of Health has recorded several cases where eating large numbers of apricot kernels have caused illness (but not deaths), and this illness has been attributed to *amygdalin* by some persons, although not by the California State Department of Health. The types of apricot kernels available in California contain 1% to 2% amygdalin, the rest of the kernel being composed of proteins, enzymes, fats, cellulose, lignin and other natural chemical compounds. It would be jumping to conclusions to conclude that the illness referred above was caused by amygdalin instead of one or more of the other chemical compounds in apricot kernels. In other words one has to make a distinction between the essentially zero toxicity of pure amygdalin and the potential toxicity of complex natural substances.

One personal reason that leads me to believe that *amygdalin* is non-toxic is that for several years I have taken 1 gram of pure amygdalin per day (500 milligrams enough amygdalin for good health. One gram of pure amygdalin is equivalent to about 250 almond kernels. Also, I eat apricot kernels, almonds and buckwheat both for flavour and for their amygdalin contents.

/s/ Raymond Ewell  
RAYMOND EWELL, PH.D.  
Date—Dec. 13, 1976

REPUBLIC OF AUSTRIA       )  
 CITY OF VIENNA            )  
                                   ) SS  
 EMBASSY OF THE            )  
 UNITED STATES OF AMERICA )

Subscribed and sworn to before me Richard E. Schroeder, Vice Consul of the United States of America in and for Austria, duly commissioned and qualified, this 13th day of Dec., 1976.

/s/ Richard E. Schroeder  
 RICHARD E. SCHROEDER  
 American Vice Consul

[SEAL]

IN THE UNITED STATES DISTRICT COURT  
 WESTERN DISTRICT OF OKLAHOMA

No. CIV 75-0218-B

GLEN L. RUTHERFORD, individually and on behalf of  
 a class composed of terminally ill cancer patients,  
 PLAINTIFFS

v.

UNITED STATES OF AMERICA, JOSEPH A. CALIFANO, Secretary of Health, Education, and Welfare; DONALD KENNEDY, Commissioner of the Food and Drug Administration, *et al.*, DEFENDANTS

AFFIDAVIT OF GERALD M. RACHANOW

Gerald M. Rachanow, being duly sworn, deposes and says:

1. I am a Consumer Safety Officer in the Bureau of Drugs, Office of Compliance, United States Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland.

2. I have reviewed the physician's affidavits intended to support the importation of Laetrile for delivery to and the personal use of sixteen persons. These affidavits designate Cyto Pharma U.S.A., 146 Main Street, Suite 405, Los Altos, California 94022, and various treating physicians as the patients' duly designated agents for the purposes of importation and interstate transportation of the Laetrile. The sixteen affidavits are for a total of 2146 3-gram vials and 9600 500 mg. tablets of Laetrile. The import shipment is identified as entry number 127199. Copies of the sixteen affidavits are attached hereto as Exhibit 1.

3. On August 12, 1977, instructions were given to FDA district offices to contact these sixteen patients and to ascertain whether the patients had received all or any of the Laetrile ordered; how much, if any, of the order



was outstanding; and how much of the Laetrile they desired to receive now.

\* \* \* \*

5. FDA investigators were able to contact all of the patients or members of their families except one, and the investigators either obtained a signed statement (affidavit) or prepared memoranda in the usual course of business recording what transpired.

\* \* \* \*

7. Of particular interest is the information obtained from Herman Dillingham, son of Aaron Dillingham. He stated that he placed an order for 56 ampoules for his father in July 1977 and that he paid \$588.00 (\$10.50 per ampoule) in advance to cover the whole shipment from Mexico. He did not mention ordering any tablets, yet the physician's affidavit indicates that 750 tablets were ordered. Further, the physician's affidavit is signed in the name of Aaron Dillingham and indicates that the physician conducted a thorough medical examination of the patient on July 8, 1977. Since the son has stated that he placed the Laetrile order for his father, we cannot establish that a bona fide physician-patient relationship existed in this case.

The motives of the supplier are also in question as regards this patient. When contacted by telephone on August 11, 1977 by a person representing the agent, Cyto Pharma, U.S.A. (Los Altos, California), Herman Dillingham indicated that he did not wish to receive any tablets; however, the Cyto Pharma, U.S.A., representative stated to him that his father may need the tablets also at a later date so they would get the entire order as originally placed. (See Exhibit 3).

\* \* \* \*

9. Some of the information obtained from these patients or their families is of particular interest. Mabel Gulbrandson's sister informed the investigator that she has been using Laetrile for about 15 months and receives it on a regular basis. From the sister's comments, it appears difficult to ascertain whether or not this patient is using the injectable Laetrile. (See Exhibit 5).

10. J. M. Richards', Jr., wife signed an affidavit that a 2½ month supply of Laetrile consisting of 300 tablets was purchased while in Ponca City, Oklahoma on June 6, 1977. It should be noted that the affidavit purportedly intended for this shipment was dated June 6, 1977 (for 150 vials and 650 tablets), that the 300 tablet supply of Laetrile tablets was purchased on June 6, 1977 and that Mrs. Richards does not mention any order being outstanding. (See Exhibit 13).

11. J. B. Gray provided an affidavit stating that in June 1977 he went to the Gibson Clinic in Ponca City, Oklahoma and upon his return home (in June 1977) he brought with him a six month supply of Laetrile. He further stated that he does not intend to reorder until December 1977 and that he does not want any of the Laetrile ordered via the affidavit dated June 1, 1977. It should also be noted that Mr. Gray stated that he signs all legal documents as "Jasper B. Gray" and that he has no idea how the signature J. B. Gray appeared on the June 1, 1977 Laetrile affidavit. (See Exhibit 14).

\* \* \* \*

13. Thelma Brashear signed an affidavit that she received a four month supply of Laetrile tablets (around July 1, 1977) when she completed treatment at the Gibson Clinic in Ponca City, Oklahoma and that she has no outstanding order. Although her affidavit calls for 150 vials and 650 tablets as a six month supply, she stated that she received only a four month supply of tablets and there is no mention of receiving any vials. (See Exhibit 15).

\* \* \* \*

19. From the above stated facts, it appears that very little of the Laetrile covered by these sixteen affidavits is intended for delivery to or the personal use of the patients identified in the affidavits. It would appear that this Laetrile supply would constitute an inventory from which the agents involved could supply Laetrile to other patients, with or without an affidavit, there being no way to control such substitute consignment.

20. It appears that at least one designated agent, a treating physician, e.g., Robert W. Gibson, M.D., Ponca

City, Oklahoma, has been maintaining an inventory of Laetrile and furnishing it to patients at his clinic in Ponca City when the patients visit him. (See Exhibits 12, 13, 14, 15 and 16). It further appears that the Laetrile is provided to the patients near the time that the affidavit for importation is executed, prior to the affidavit ever being provided to Customs officials to "legally" import the Laetrile.

21. One patient's wife, Mrs. Kenneth Wilson, stated to the investigator that most of the tablets which her husband could not take were returned to the supplier. Did these tablets then form part of an inventory? Were they subsequently provided to another patient? There appears to be no way of knowing about or monitoring occurrences of this type.

I certify under penalty of perjury that the foregoing statement is true and correct. Done this 18th day of August, 1977.

/s/ Gerald M. Rachanow  
GERALD M. RACHANOW  
Consumer Safety Officer

EXCERPT FROM THE TRANSCRIPT OF ORAL  
ARGUMENT BEFORE THE COMMISSIONER  
May 22, 1977

[311] Well, actually, you are going to go back and prepare your foods just exactly like your great-great grandparents prepared their foods. And they had every bit of the stuff and they were alive and they didn't have cancer.

(Applause.)

MR. RUTHERFORD: In January or March of 1972, I wrote the following paragraph. It went to my Congressman; it went to my Senators. I got very few answers.

I said, "The Federal Food and Drug Administration has known about laetrile since 1940. Yet in all this time, FDA has refused to produce specific tests conducted by the FDA in regards to laetrile. The FDA has consistly refused to allow the use or the testing of laetrile by anyone, even on an experimental basis, in the United States. The FDA says that it is a poison. I have been on the laetrile program since December 22, 1970 with no side effects until the present moment. I inject anywhere from one 500 milligram tablet or 1/2 gram to as high as nine of them in a day's time depending on what this carcass is telling me and I've learned to read the signals about what my body does tell me.

"May I remind the FDA that cobalts, cytoxin and all the chemotherapeutic drugs are all deadly in their own right. But the FDA allows them to be used. Why?"

SUPREME COURT OF THE UNITED STATES

No. 78-605

UNITED STATES, ET AL., PETITIONERS

v.

GLEN L. RUTHERFORD, ET AL.

ORDER ALLOWING CERTIORARI

Filed January 22, 1979

The petition herein for a writ of certiorari to the United States Court of Appeals for the Tenth Circuit is granted.



JAN 2 1979

MICHAEL RÓDÁK, JR., CLERK

*In the Supreme Court of the United States*

OCTOBER TERM, 1978

**No. 78-605**

UNITED STATES OF AMERICA, ET AL.,

*Petitioners,*

V E R S U S

GLEN L. RUTHERFORD, ET AL.,

*Respondents.*

**RESPONSE BRIEF TO PETITION FOR WRIT OF  
CERTIORARI TO THE UNITED STATES COURT  
OF APPEALS FOR THE TENTH CIRCUIT**

KENNETH RAY COE, of the firm  
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Oklahoma City, Oklahoma 73102

*Counsel for Respondents*

January, 1979

In the  
Supreme Court of the United States

OCTOBER TERM, 1978

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No. 78-605

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UNITED STATES OF AMERICA, ET AL.,  
*Petitioners,*

V E R S U S

GLEN L. RUTHERFORD, ET AL.,  
*Respondents.*

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**RESPONSE BRIEF TO PETITION FOR WRIT OF  
CERTIORARI TO THE UNITED STATES COURT  
OF APPEALS FOR THE TENTH CIRCUIT**

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**SCOPE OF BRIEF**

This Brief is in response to the Petition for Writ of Certiorari to the United States Court of Appeals for the Tenth Circuit, filed by the Solicitor General on behalf of the United States.

**ISSUES**

The Petition for Certiorari lists the question presented for review as follows:

“Whether the safety and effectiveness requirements of the Federal Food, Drug, and Cosmetic Act apply to drugs intended for use by the terminally ill.”

Although it is difficult to clearly delineate the issues presented by the United States as reasons for granting the Petition to resolve the question presented, the following appear to be the issues:

1. The decision of the Court of Appeals is contrary to the meaning of the Food and Drug Act.
2. The Appeals Court decision limits the Commissioner's power to protect the public from unsafe and ineffective drugs.
3. The decision by the Appeals Court would prevent the Commissioner from concluding that any drug intended for use by the terminally ill has not been shown to be safe and effective.
4. The Appeals Court decision would make it difficult for the Commissioner to discharge his statutory responsibility to keep unproven drugs out of the marketplace.
5. As a separate basis, the United States argues that the Appeals Court decision is inconsistent with the decision in *Rutherford v. American Medical Ass'n*, 379 F.2d 641 (7th Cir. 1967, cert. denied, 389 U.S. 1043 (1968)).

#### **ARGUMENT AND AUTHORITIES**

Initially, this Brief will deal with the purported inconsistency of Circuit Court opinions.

In the case *Rutherford v. American Medical Ass'n*, supra, an action was brought seeking an injunction against the Food and Drug Administration to order it to cease interfering with distribution of the drug Kreboizen.

The Court pointed out that there had been no attempted compliance with the Food, Drug and Cosmetic Act and therefore, that the Court did not have jurisdiction:

"Without an attempted good faith application for approval or exemption, we have no jurisdiction to determine whether the FDA has illegally placed impossible or unreasonable conditions on approval or exemption, or has made requests for information impossible to fulfill, or whether the FDA has been dilatory, biased, or discriminatory."

In the instant case there has been a good faith application to the Food and Drug Administration. As pointed out in the Petition for Certiorari of the United States, this case was appealed to the Tenth Circuit Court of Appeals on one earlier occasion and at that time, the Tenth Circuit ruled that the preliminary injunction previously granted would remain in effect; however, the Court was of the opinion that there was probably no administrative record prepared by the FDA to support its conclusion that Laetrile was a "new drug." The Circuit Court of Appeals then ordered the District Court to remand the case to the FDA for proper administrative proceedings if the same were necessary.



In a later hearing before the Honorable Judge Luther Bohanon, the attorneys for the Food and Drug Administration stipulated that there was no administrative record and the case was subsequently remanded to the FDA. The Commissioner of the Food and Drug Administration published notice in the Federal Register of an administrative proceeding on Laetrile and also conducted two days of hearings in Kansas City.

After an immense record was amassed, the Commissioner issued his order finding that Laetrile was not exempt from the Act and that it should not be shipped in interstate commerce.

The Food and Drug Administration cannot complain that it was not given opportunity to conduct the initial administrative proceeding in regard to Laetrile. The United States District Court for the Western District of Oklahoma reviewed the entire administrative record and issued its order, setting that opinion aside. This decision has been affirmed by the Tenth Circuit Court of Appeals.

The entire basis for the Court's decision in *Rutherford v. American Medical Ass'n*, supra, was that the initial jurisdiction was in the FDA rather than the courts. In this case, the FDA has had opportunity to exercise initial jurisdiction and to make its administrative finding. That administrative finding is subject to judicial review: *Weinberger v. Henson*, *Westcott and Dunning*, 412 U.S. 609 (1973). In addition, the administrative decision to be affirmed must not be arbitrary, capricious or abusive of agency discretion; *Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 416 (1971).

The District Court for the Western District of Oklahoma, upon reviewing the administrative record, concluded:

"Such decision is arbitrary, capricious, that it represents an abuse of discretion and is not in accordance with law. Consequently, it must be set aside and vacated."

The District Court did nothing it was not empowered to do and the Circuit Court of Appeals acted properly in affirming the District Court's decision.

Now we will turn our attention to the other arguments raised by the United States, those being primarily difficulties the agency will have if it is forced to abide by the Tenth Circuit ruling, and that the decision is contrary to the clear meaning of the Act.

A proper response to these arguments is best predicated upon a statement of the limitations imposed in the Tenth Circuit's Order. The Order of the Tenth Circuit contains the following explicit limitations:

1. The ruling applies only to "terminal" cancer patients.
2. The ruling applies only to Laetrile.
3. The ruling applies only to the liquid form of Laetrile.

Also to be considered is the fact that the FDA conducted an extensive administrative proceeding on the drug Laetrile before the District Court for the Western District of Oklahoma ruled upon the record and the Tenth Circuit Court of Appeals affirmed the District Court's decision.

Finally, consideration must be given to the fact that the term "life threatening" and "terminal" are not synonymous. There are many "life threatening" diseases for which there is an adequate remedy. There are no "terminal" diseases for which there is an adequate remedy; hence, the term "terminal."

The Government's Petition for Certiorari does not set out in detail the problems it anticipates in enforcing the Act if the decision of the Tenth Circuit stands. It merely says in conclusory terms that problems will exist.

It is difficult to fathom the problems the Commissioner will face when any other substance will have to withstand the same administrative and judicial review that Laetrile faced before any decision like this one could be rendered. The agency was not denied its right of administrative review and that administrative review is all that the Food, Drug and Cosmetic Act requires of the FDA.

The argument that the decision is contrary to the plain meaning of the Statute is spurious. Neither the Statute nor any cases cited thereunder have dealt with a specific class of "terminal" patients and the application of one specific substance (here Laetrile).

There is no question that the Food and Drug Administration is empowered to prevent unsafe and ineffective substances from reaching the general public; however, the extent of the FDA's power is not nearly so clearly established as the FDA asserts.

Both the District Court and the Tenth Circuit Court have faced the same problems in interpreting the duties of

the FDA in respect to "terminal" cancer patients. Both courts have had extreme difficulty in resolving the applicability of the terms "safe" and "effective" to an individual who has already heard the death knell from his doctor. For those patients there is certainly no orthodox "effective" therapy or the patient would not be classified as "terminal."

The entire administrative record is bereft of any bona fide evidence that Laetrile is not "safe." Laetrile has been administered to tens of thousands of Americans, both in this country and in Mexico and there is not a single case of an individual being harmed by administration of Laetrile. The closest the FDA came to a safety issue was the assertion that certain individuals who had eaten apricot pits had suffered adverse reaction. Laetrile is not apricot pits but a derivative thereof. Additionally, there was no showing that the individuals who took the apricot pits were even cancer patients.

Neither the decision of the Circuit Court of Appeals nor the decision of the District Court for the Western District of Oklahoma impairs, in any way, the authority or prerogatives of the Food and Drug Administration. The Food and Drug Administration was given its opportunity to conduct its administrative proceeding. The fact that the administrative decision was overturned within the discretion of the reviewing court and the fact that the Food and Drug Administration has lost its case to this point does not mean that it has lost its administrative prerogatives. If the decisions of the Food and Drug Administration were not subject to being overturned, there would be no need for the judicial review provided.

**CONCLUSIONS**

For the reasons stated above, the Petition for the Writ of Certiorari by the United States Government should be denied.

Respectfully submitted,

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December, 1978



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No. 78-605

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**In the Supreme Court of the United States**  
**OCTOBER TERM, 1978**

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**UNITED STATES OF AMERICA, ET AL., PETITIONERS**

*v.*

**GLEN L. RUTHERFORD, ET AL.**

---

**ON WRIT OF CERTIORARI TO THE UNITED STATES  
COURT OF APPEALS FOR THE TENTH CIRCUIT**

---

**BRIEF FOR THE UNITED STATES**

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## In the Supreme Court of the United States

OCTOBER TERM, 1978

No. 78-605

UNITED STATES OF AMERICA, ET AL., PETITIONERS

v.

GLEN L. RUTHERFORD, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES  
COURT OF APPEALS FOR THE TENTH CIRCUIT

### BRIEF FOR THE UNITED STATES

#### OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-7a) is reported at 582 F.2d 1234. The opinion of the district court (Pet. App. 11a-44a) is reported at 438 F. Supp. 1287. The decision of the Commissioner of Food and Drugs (Pet. App. 45a-274a) is reported at 42 Fed. Reg. 39768.

#### JURISDICTION

The judgment of the court of appeals (Pet. App. 8a-9a) was entered on July 10, 1978. On August 4,



1978, the court of appeals summarily denied a Motion for Clarification or in the alternative Petition for Re-Hearing filed by respondents (Pet. App. 10a). The petition for a writ of certiorari was filed on October 10, 1978, and granted on January 22, 1979. The jurisdiction of this Court rests on 28 U.S.C. 1254(1).

### QUESTIONS PRESENTED

1. Whether the safety and effectiveness requirements of the Federal Food, Drug, and Cosmetic Act apply to drugs intended for use by the terminally ill.

2. Whether the judgment of the court of appeals barring application of the Federal Food, Drug, and Cosmetic Act to interstate distribution of the drug Laetrile for intravenous administration to terminally ill cancer patients is sustainable on the ground that Laetrile is exempt from the premarketing clearance requirements of the Act by operation of the Act's 1962 grandfather clause.

3. Whether the judgment of the court of appeals is sustainable on the ground that prohibition of the interstate distribution of Laetrile violates a constitutional right of privacy.<sup>1</sup>

<sup>1</sup> Questions 2 and 3 are issues reached by the district court but not by the court of appeals. As we noted in our petition for certiorari (Pet. 18), respondents can be expected to argue that the judgment of the court of appeals should be affirmed on the grounds relied on by the district court. See *United States v. New York Telephone Co.*, 434 U.S. 159, 166 n.8 (1977). For that reason we address those issues here. In view of the importance of this case to the federal system of drug regulation and the need to secure a final resolution of the issues after four years of litigation, we urge the Court to decide all of the issues here in the event it concludes that the court of appeals' reasoning is erroneous.

### STATUTES INVOLVED

The pertinent portions of Sections 201(p) and 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321(p) and 355, and Section 107(c)(4) of the Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 789 ("1962 grandfather clause"), are reproduced at Pet. 2-5.

### STATEMENT

#### A. Initial Court Proceedings

Section 505 of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 355, prohibits the interstate distribution of any "new drug," as defined in Section 201(p) of the Act, 21 U.S.C. 321(p), unless (1) a new drug application (NDA), supported by appropriate evidence of the drug's safety and effectiveness, has been approved by the Secretary of Health, Education and Welfare, or (2) the drug is exempted from the approval requirements by one of the Act's two "grandfather" provisions.<sup>2</sup> The Secre-

<sup>2</sup> Under the 1938 Act, a "new drug" was one not generally recognized by qualified experts as safe for its intended use (Section 201(p), 52 Stat. 1041). The Act contained a "grandfather clause" excluding from the definition of "new drug" any drug which, before enactment of the 1938 Act, was subject to the Pure Food and Drugs Act of 1906 (ch. 3915, 34 Stat. 768), and for which representations concerning the conditions of use were identical to those made for its use before the 1938 Act was enacted. This 1938 grandfather clause remains in the current Act. 21 U.S.C. 321(p)(1).

The 1962 Amendments also contain a grandfather clause, excluding from the definition of "new drug" any drug that, on October 9, 1962 (the day immediately preceding the enact-

tary has delegated his approval authority to the Commissioner of Food and Drugs (the Commissioner), who directs the Food and Drug Administration (FDA). 21 C.F.R. 5.1(a)(1).

This case concerns a group of drugs that differ in chemical composition but are known, or have been known, by the name Laetrile (Pet. App. 58a-69a).<sup>3</sup> Alleging that the proponents of Laetrile in its various forms had not established either that it was entitled to grandfather status or that it met the statutory requirements for approval as a new drug, the FDA brought a series of civil and criminal actions to prevent the introduction of Laetrile, under various names and in various forms, into interstate commerce.<sup>4</sup>

ment of the 1962 Amendments): "(A) was commercially used or sold in the United States, (B) was not a new drug [under the 1938 Act] \* \* \*, and (C) was not covered by an effective [new drug] application." Section 107(c)(4), 76 Stat. 789.

<sup>3</sup> Some of these drugs have also been known by other names—for example, "amygdalin" (see discussion at pages 6-7, *infra*). For the sake of convenience we will use only the name Laetrile, unless discussion of a particular point requires distinguishing among different names or formulations.

<sup>4</sup> *E.g.*, *United States v. Turner*, 558 F.2d 46 (2d Cir. 1977) (criminal prosecution for conspiracy to import Laetrile); *United States v. Westover*, 511 F.2d 1154 (9th Cir.), cert. denied, 422 U.S. 1009 (1975) (criminal prosecution for conspiracy to import); *United States v. Articles of Food and Drug*, 449 F. Supp. 497 (E.D. Wisc. 1978) and 441 F. Supp. 772 (E.D. Wisc. 1977) (civil seizure action); *United States v. Spectro Foods Corp.*, Civ. No. 76-101 (D. N.J. Jan. 29, 1976), *aff'd* in pertinent part, 544 F.2d 1175 (3d Cir. 1976) (civil injunctive suit); *United States v. General Research Laboratories*, 397 F. Supp. 197 (C.D. Cal. 1975) (civil in-

In March 1975, respondents instituted the present suit to enjoin the government from interfering with the sale and distribution of Laetrile by the filing of additional injunctive, seizure, or criminal actions (A. 7-11).<sup>5</sup> In August 1975 the district court issued a preliminary injunction that enjoined the government from preventing the purchase and subsequent interstate movement of a limited quantity of Laetrile for Glen L. Rutherford, one of the plaintiffs (A. 18-19).<sup>6</sup> The court of appeals did not disturb this injunction, but instructed the district court to remand the case to the Commissioner for the development of an adminis-

junctive suit). Earlier unreported decisions are published in the Drug and Device Notices of Judgment (D.D.N.J.) published by the FDA under the authority of 21 U.S.C. 375(a). See, *e.g.*, *United States v. An Article of Drug . . . Laetrile (Krebs Laboratories) etc.* (D. Ida. Apr. 30, 1965), D.D.N.J. No. 8507 (Sept. 1966) (civil condemnation suit); *United States v. Hawk et al.* (S.D. Cal. Feb. 23, 1963), D.D.N.J. No. 8082 (July 1965) (civil injunctive suit).

<sup>5</sup> The suit was originally instituted by Juanita Stowe, a cancer patient, and her husband Jimmie Stowe. After Mrs. Stowe's death, an amended complaint was filed by two other patients, Glen L. Rutherford and Phyllis S. Schneider, and Mrs. Schneider's husband, on behalf of a class composed of cancer patients and their spouses who are responsible for the costs of treatment. Mrs. Schneider subsequently died. By order entered April 8, 1977, the district court certified this case as a class action on behalf of a class composed of terminally ill cancer patients (A. 47-58). That order was not appealed by the government.

<sup>6</sup> The district court subsequently entered similar orders on behalf of others who showed, by affidavit, that they were members of the certified plaintiff class of terminally ill cancer patients (A. 1-6).

trative record addressing the issues whether Laetrile is a new drug within the meaning of Section 201(p) of the Act and, if so, whether it is exempt from the premarketing approval requirements by virtue of either the 1938 or the 1962 grandfather clause (A. 31-41).

#### B. Administrative Proceedings on Remand

The Commissioner initiated administrative proceedings through a Federal Register announcement seeking public comment, and provided individual notice to certain interested persons known to be Laetrile proponents (Pet. App. 47a-49a; 42 Fed. Reg. 10066-10069 (1977)). The proceedings included two days of public hearings and produced more than four hundred submissions, totaling more than five thousand pages, from diverse sources. On July 29, 1977, the Commissioner issued his opinion (Pet. App. 45a-274a).

1. The Commissioner found that the controversy concerns a number of different drugs (*i.e.*, drugs consisting of different chemical compounds) that are referred to by a number of different names, including "Laetrile," "laetrile(s)," "amygdalin," and "vitamin B-17" (Pet. App. 58a-73a). The drugs either consist at least in part of a specific chemical compound known as "amygdalin" (a glucoside present in the kernels or seeds of most fruits) or are related in some way to that compound (Pet. App. 58a-59a, 62a-66a). The proper chemical name for amygdalin is D-mandelonitrile-*beta*-D-glucosido-6-*beta*-D-glucoside

(Pet. App. 63a). Amygdalin thus differs in chemical structure from a compound that Ernst T. Krebs, Jr., prepared in 1952 and named "Laetrile" (Pet. App. 63a-64a). That compound was identified by Krebs, one of the proponents of Laetrile, as a substance for which the chemical name is l-mandelonitrile-*beta*-glucuronoside (Pet. App. 65a). Despite the difference in chemical structure, proponents and opponents of the drugs in controversy have used the terms "laetrile" and "Laetrile" interchangeably with the term "amygdalin" for the compounds described above and even for somewhat different compounds (Pet. App. 66a, 69a). The Commissioner concluded that there is no uniform definition of the proper noun "Laetrile" (Pet. App. 69a) and that the term "laetrile" is in practice a "broad or generic term for a group of compounds of unknown number" (Pet. App. 70a). Chemical identification of a particular drug is essential to proving claims that it is not a new drug, that it comes within one of the grandfather clauses of the Act, or that it meets safety and effectiveness requirements for new drugs (Pet. App. 104a, 166a, 180a-181a).

2. The Commissioner concluded that Laetrile in its various forms is a "drug" as defined in the Act, because it is being sold for the cure or prevention of disease within the meaning of Section 201(g)(1) of the Act, 21 U.S.C. 321(g)(1) (Pet. App. 245a-247a). In determining whether Laetrile is a "new drug"—*i.e.*, one not generally recognized by qualified experts as safe and effective for its suggested use (Section



201(p) of the Act, 21 U.S.C. 321(p))—the Commissioner applied the statutory criteria recognized by this Court in *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 629-632, 652 (1973). The Commissioner reviewed the record both for controlled investigations, conducted by qualified experts and published in the scientific literature, establishing the safety and effectiveness of the drug, and for the views of experts, based on that evidence, that the drug is safe and effective (Pet. App. 89a-93a).

A review of the scientific literature throughout the world failed to produce reliable information from which experts could make a determination concerning Laetrile's safety (Pet. App. 155a-157a). Experts testified that there were no adequate scientific studies of the safety or toxicity of Laetrile in any method of administration, either when taken alone or in conjunction with other cancer drugs (Pet. App. 155a-157a, 271a). They testified that there were, nonetheless, definite indications that oral administration of Laetrile is toxic (*id.* at 157a-162a; see *id.* at 254a-257a), a danger that Laetrile's proponents had themselves recognized in their earlier labeling of the drug (*id.* at 86a-88a, 158a, 254a-255a).<sup>7</sup>

<sup>7</sup> Documents relating to FDA reviews of applications submitted in 1962 and 1970 for approval of the use or marketing of Laetrile were included in the record. On October 3, 1962, Ernst T. Krebs, Jr., submitted NDA's for two Laetrile formulations to be administered in a series of injections for the treatment of cancer (Pet. App. 191a-192a, 197a, 203a-204a). Neither was approved, because of the lack of data showing safety and effectiveness. *Id.* at 203a-204a; see page 28, note

The Commissioner accordingly found that Laetrile had not been adequately tested for safety and that it was not generally recognized among experts as safe for use in man (Pet. App. 154a-162a).<sup>8</sup>

The Commissioner reached similar conclusions with respect to the drug's effectiveness. Data submitted for the record by Laetrile proponents failed to meet the standards prescribed for controlled clinical investigations of drug effectiveness. With respect to studies on humans, the Commissioner found that "[t]here are

14, *infra*. In 1970, the McNaughton Foundation submitted a notice of claimed investigational exemption for Laetrile under which it would be allowed to conduct studies in humans. The FDA denied permission to conduct tests because the data supplied to show safety were inadequate to justify use of the drug in humans. *Id.* at 155a-156a.

<sup>8</sup> Reports appearing in the medical literature after the administrative hearing support the toxicity findings regarding oral Laetrile and raise new questions about the toxicity of the injectable form of the drug. See Humbert, et al., *Fatal Cyanide Poisoning: Accidental Ingestion of Amygdalin*, 238 JAMA 482 (1977). The authors report the death of an 11-month-old girl who accidentally ingested from one to five 500 mg. amygdalin tablets. See also Lewis, *Laetrile*, 127 West J. Med. 55 (1977), for a report on 25 cases of cyanide toxicity associated with the use of articles containing amygdalin; and Schmidt, et al., *Laetrile Toxicity Study in Dogs*, 239 JAMA 943 (1978).

For findings not limited to the oral form, see Smith, et al., *Laetrile Toxicity: A Report of Two Cases*, 238 JAMA 1361 (1977). The authors report that toxicity was associated with use of both the oral and injectable forms of Laetrile. Symptoms disappeared after Laetrile was discontinued. In one case the patient reinstituted self-medication with Laetrile against medical advice, and symptoms of rash, fever, malaise, headache and severe abdominal cramps reappeared. Laetrile was again withdrawn and the symptoms disappeared.

no clinical investigations of Laetrile's effectiveness, published or otherwise, which are even arguably adequate and well controlled" (Pet. App. 93a-94a). Case reports of physicians who used Laetrile in their practices were anecdotal and otherwise lacking in scientific control and detail (Pet. App. 100a-108a). The Commissioner also evaluated reports of tests in laboratory animals (Pet. App. 114a-126a). He found that these tests failed to show that Laetrile produces anticancer activity in such animals (Pet. App. 126a). Experts from leading medical schools and cancer research and treatment centers (see *id.* at 126a-149a) testified that there is no laboratory or clinical evidence available to support a conclusion that Laetrile is effective, and stated that they could not recognize Laetrile as effective in the absence of such evidence (Pet. App. 126a-149a).

Since the evidence established that Laetrile was not generally recognized by experts as safe and effective for its suggested use as an anticancer drug, the Commissioner concluded that it was a "new drug" under the Act (Pet. App. 163a). It followed that distribution of the drug prior to premarketing approval by the FDA would be unlawful, unless the drug qualified for exempt status under the 1938 or 1962 grandfather provision (*ibid.*).

3. Drugs that were subject to the Pure Food and Drugs Act of 1906, ch. 3915, 34 Stat. 768, and that continue to bear identical labeling concerning conditions of use, are exempted from the "new drug" provisions of the Federal Food, Drug and Cosmetic Act

by Section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1). The record evidence before the Commissioner included uncorroborated reports about the use in past centuries of substances claimed to be related to amygdalin or Laetrile (Pet. App. 167a-169a). It also included reports of experiments, beginning in the 1920's, in which Dr. Ernst Krebs, Sr., developed a drug he called "Sarcarcinase"—a drug demonstrably different in chemical structure from drugs now known as Laetrile (Pet. App. 169a-178a, 70a-73a). On the basis of all the evidence, the Commissioner concluded that not only was the record devoid of proof that "Laetrile was used and labeled before 1938 in a manner identical to its present use and labeling," but that the record affirmatively showed "that present day Laetrile was not developed until after 1938" (Pet. App. 178a-179a). He accordingly found that Laetrile does not qualify for exemption under the 1938 grandfather clause (*ibid.*).

4. The Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 789, redefined a "new drug" as one not generally recognized as both safe and effective. Section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1).<sup>9</sup> However, Section 107(c)(4) of the 1962 Drug Amendments, Pub. L. No. 87-781, 76 Stat. 789 (page 3, note 2, *supra*), exempts any drug as to which it is shown: (1) that the same drug, by chemical composition, was used or sold in the United States on October 9, 1962; (2) that the 1962 drug was

<sup>9</sup> Section 201(p) as it read prior to its amendment in 1962 is set forth at Pet. App. 180a.

commercially available at that time; (3) that the 1962 drug was at that time generally recognized by experts as safe for its intended use (and thus was not a "new drug" under the 1938 Act); (4) that the present labeling is the same as the labeling on the drug as sold on October 9, 1962;<sup>10</sup> and (5) that the 1962 drug was not then covered by an effective NDA under the 1938 Act (Pet. App. 179a-181a).

The Commissioner found that Laetrile failed to satisfy four of the five 1962 grandfather requirements.<sup>11</sup> First, the drug in use on the 1962 grandfather date and the Laetrile drugs presently in use did not have an identical composition. The composition of substances referred to as Laetrile varied, and "any drug in use on October 9, 1962 was different in composition from Laetrile as used, or proposed to be used, today" (Pet. App. 187a). Second, the use of Laetrile on the grandfather date was investigational, not commercial, because it was then used only to determine its safety and effectiveness as a cancer treatment (Pet. App. 187a-190a). Third, Laetrile could not be considered to have been generally recognized as safe on October 9, 1962, because experts were largely unfamiliar with the drug, lacked infor-

<sup>10</sup> The term "labeling" means all written, printed, or graphic matter on or accompanying the drug. 21 U.S.C. 321(m). See *Kordel v. United States*, 335 U.S. 345 (1948); *United States v. Urbuteit*, 335 U.S. 355 (1948).

<sup>11</sup> The requirement satisfied was that Laetrile was not covered by an effective new drug application on the 1962 grandfather date (Pet. App. 180a).

mation about its composition and labeled conditions of use, and, in the absence of any published literature regarding safety and effectiveness, would have had no scientific basis on which to recognize the drug as safe (Pet. App. 200a-211a). Fourth, the Commissioner determined that no labeling was described or submitted for Laetrile as a product in use on October 9, 1962, and that even if labeling in a new drug application submitted on October 3, 1962 (see page 8, note 7, *supra*) were viewed as pre-grandfather date labeling, it was not the same as the subsequent labeling and suggested conditions of use (Pet. App. 191a-199a).<sup>12</sup>

#### C. The District Court's Decision After Remand

The district court sustained the Commissioner's finding that Laetrile is a new drug because it is not generally recognized as safe and effective (Pet. App. 19a-22a). The court also left undisturbed the Commissioner's denial of an exemption under the 1938 grandfather clause (Pet. App. 35a). The court concluded, however, that Laetrile qualified for exemption under the 1962 grandfather clause, and it set aside each of the Commissioner's factual findings on this issue (Pet. App. 25a-34a).

<sup>12</sup> The Commissioner relied on a variety of sources to determine how Laetrile was labeled (Pet. App. 191a-199a). Evidence of record demonstrated a wide variance in the indications, conditions of use, dosage form, and manner of administration for Laetrile both before and after 1962 (*ibid.*). See discussion at pages 49-50, *infra*.



The district court found, first, that Laetrile and amygdalin are the same substance, having the chemical formula that the Commissioner used to describe amygdalin alone (Pet. App. 26a n.17). Second, the court concluded that the commercial use of Laetrile as a pharmaceutical product prior to the 1962 grandfather date was established by the availability of amygdalin from chemical supply houses (Pet. App. 29a-30a n.21). Third, from its review of the record the court concluded that prior to 1962 "Laetrile was generally recognized as safe" (Pet. App. 33a & n.24). And fourth, the court determined that labeling proposed for use on an unmarketed drug for which a new drug application was filed on October 3, 1962, established conditions of use on October 9, 1962, and that the present drug qualified for grandfather status to the extent that it bore the same labeling (Pet. App. 15a n.7) (see page 8, note 7, *supra*).

The court also held that by "denying the right to use a nontoxic substance in connection with one's own personal health-care, FDA has offended the constitutional right of privacy" (Pet. App. 41a (footnote omitted)). This holding incorporated a rejection of the evidence credited by the Commissioner that Laetrile has a known toxicity that has not been adequately investigated (Pet. App. 157a-162a, 254a-257a; compare Pet. App. 30a-31a & n.23, and 33a n.24), and a rejection of the Commissioner's factual findings, based on that evidence, that Laetrile is not generally recognized among experts as safe for use in man (Pet. App. 157a).

#### D. The Decision of the Court of Appeals

The court of appeals, without addressing either the statutory or the constitutional ground on which the district court relied, held "as a matter of law that the 'safety' and 'effectiveness' terms used in the statute have no reasonable application to terminally ill cancer patients" (Pet. App. 3a). The FDA had failed, in the court's view, to advance a standard against which to measure the safety and effectiveness of Laetrile with respect to such patients and had therefore erroneously applied the Act (Pet. App. 6a). The court emphasized that its decision applied only to the intravenous use of Laetrile by terminally ill cancer patients, a group whose members, it concluded, could be identified without difficulty by the certification of a licensed medical practitioner (Pet. App. 5a-6a). The permanent injunction entered by the district court was continued as modified, and the FDA was directed "to promulgate regulations" within the circuit court's guidelines "as if the drug was found by the Commission[er] to be 'safe' and 'effective' for the limited group of persons here considered" (Pet. App. 7a).

#### SUMMARY OF ARGUMENT

##### I

The Federal Food, Drug, and Cosmetic Act defines a "new drug" as one not generally recognized by qualified experts as safe and effective for its recommended use. 21 U.S.C. 321(p)(1). The Act provides that "[n]o person shall introduce or deliver for in-

troductio into interstate commerce any new drug \* \* \* unless a new drug application is effective for that drug, and requires that before a new drug application is approved the drug must be proved to be safe and effective. 21 U.S.C. 355(a), (d). In holding that the safety and effectiveness requirements of the Act do not apply to drugs intended for use by the "terminally ill," the court of appeals has disregarded all relevant guides to statutory construction, including the language of the Act, the purpose it embodies, and the interpretation consistently and reasonably placed on it by the agency charged with enforcing it.

The Act provides certain express exceptions from its safety and effectiveness requirements, but there is no exception for drugs to be used by the "terminally ill." The legislative histories of both the 1938 Act, in which the safety requirement was imposed, and the 1962 amendments, in which the effectiveness requirement was imposed, indicate that Congress specifically intended to make these requirements applicable to drugs for the treatment of cancer, including cancer in its last stages. The Food and Drug Administration, in enforcing both the safety and effectiveness requirements, has never made an exception for drugs to be administered to the terminally ill, and Congress has indicated its acquiescence in this administrative construction.

The Act's standards of safety and effectiveness are not meaningless as applied to drugs to be used by patients who are "terminally ill" with cancer. In the first place, the Commissioner reasonably found that

there is no reliable means of identifying that class of patients, except in retrospect; hence any group so identified can be expected to include some patients who will respond positively to conventional cancer therapies, and for these patients the Act's standards are surely applicable. But even for those who are indeed beyond cure, the standards have meaning. A drug is "unsafe" for such patients, as for anyone else, if it poses risks of shortening life expectancy or aggravating symptoms that are not outweighed by potential benefits of prolonging life, improving health, or ameliorating pain. A drug is "ineffective" for such patients, as for anyone else, if it does not produce the effects of prolonged life expectancy, improved health, or reduced pain that are claimed for it.

The "terminally ill" have as much interest as the general public in the protection that Congress has sought to provide against drugs that are not both safe and effective. Indeed, as the Commissioner noted, the vulnerable psychological state of cancer patients may make them particularly susceptible to unfounded claims and thus create a special need for protection from ineffective drugs. The court of appeals, in holding the statutory standards inapplicable to the "terminally ill," has substituted its judgment for that of Congress and the Commissioner. And although the present case involves only the use of Laetrile under designated conditions, the reasoning of the court of appeals would prevent the Commissioner from concluding that any drug intended for use by the terminally ill has not been shown to be safe and effective,

thereby impeding if not preventing him from discharging his statutory responsibility to keep unproven drugs out of the marketplace.

## II

The 1962 amendments to the Federal Food, Drug, and Cosmetic Act include a grandfather clause that permits the continued marketing—without compliance with the effectiveness requirement established by those amendments—of certain established drugs that were being lawfully marketed in 1962 on the basis of general recognition that they were safe for their recommended uses. The Commissioner found that Laetrile does not qualify for exemption under the 1962 grandfather clause because it fails to meet four of the five requirements for such exemption. The district court reversed the Commissioner's findings and held that Laetrile is exempt under the 1962 grandfather clause. This was error.

Those seeking to qualify a drug for exemption under the 1962 grandfather clause must establish: (1) that the present drug is chemically identical to a drug in existence on the grandfather date in 1962; (2) that the drug was commercially available in 1962; (3) that the drug was at that time generally recognized by experts as safe for its intended use; (4) that the present labeling for the drug is the same as the labeling used for it in 1962; and (5) that the drug was not covered in 1962 by an effective new drug application under the 1938 Act.

Those now seeking to qualify Laetrile under the 1962 grandfather clause do not claim to have marketed the drug commercially on or before the 1962 grandfather date, and therefore lack the reliance interest that the clause is designed to protect. What is more important, the record amply supports the Commissioner's findings that the proponents of Laetrile failed to meet all but the last of the five requirements, and therefore failed to show that Laetrile qualifies for the exemption. Because the Commissioner's findings are supported by substantial evidence and are not arbitrary or capricious, they are entitled to stand. *Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 413-414 (1971). The district court's contrary conclusion, reached by an improper reweighing of the scientific evidence, is erroneous and does not provide a ground for sustaining the judgment of the court of appeals.

## III

The district court held that "[b]y denying the right to use a nontoxic substance in connection with one's own personal health-care, FDA has offended the constitutional right of privacy" (Pet. App. 41a; footnote omitted). This holding also is erroneous and affords no ground for affirming the decision of the court of appeals.

1. The district court's holding is premised on its unwarranted belief, contrary to the well-supported findings of the Commissioner, that Laetrile has been shown to be nontoxic. The court reached its conclusion by an improper reweighing of the record evidence. It relied heavily on the anecdotal experiences



of a handful of Laetrile practitioners and discounted the testimony of experts, credited by the Commissioner, which indicated that Laetrile is toxic in its oral form and that it has not been adequately tested for toxicity in any form.

2. Even if Laetrile were not toxic, there is no constitutional right to take any particular drug or class of drugs for medical purposes. The assertion of such a right challenges not only the Commissioner's ruling in this case but the Federal Food, Drug, and Cosmetic Act itself, as well as the centuries-old Anglo-American tradition of government protection of the public from foods and drugs that are unsafe, worthless, or fraudulent.

The district court perceived the asserted right as included within the constitutional right of privacy recognized by decisions of this Court beginning with *Griswold v. Connecticut*, 381 U.S. 479 (1965). In particular, the district court relied on a line of cases that this Court has characterized as protecting the individual's interest in making independent decisions in "matters relating to marriage, procreation, contraception, family relationships, and child rearing and education." *Whalen v. Roe*, 429 U.S. 589, 600 n.26 (1977), quoting *Paul v. Davis*, 424 U.S. 693, 713 (1976).

A right of caring for one's health by obtaining a particular drug without government hindrance does not fall within any of those categories and does not involve the kind of decision with which those cases were concerned. On the contrary, the Court's reason-

ing in that line of cases leads to rejection of the constitutional claim here. In *Roe v. Wade*, 410 U.S. 113 (1973), and other cases involving abortion and contraception laws, where the Court has upheld a right of privacy in matters relating to marriage and procreation, it has at the same time made it quite clear that that right may be restricted in the interest of protecting the health of the persons concerned. This recognition is inconsistent with the claimed constitutional right of access to drugs that fail to meet the requirements of a statutory system aimed at protecting the public health by assuring that marketed drugs are safe and effective for their intended uses.

The conclusion that the Constitution guarantees no right of access to ineffective drugs draws further support from this Court's opinion in *Whalen v. Roe*, *supra*, 429 U.S. at 603. The Court there stated that a state "no doubt could prohibit entirely" the use of the class of drugs involved in that case—drugs that "have accepted uses in the amelioration of pain and in the treatment of [various diseases]" but that are subject to abuse (*id.* at 593 n.8). It follows a fortiori that the government may prohibit interstate commerce in a drug that has no recognized medical use for the life-threatening disease for which it is recommended, and that has a potential for harming, at the least, those patients who are deterred by the drug's availability from seeking effective treatment.

The logic of the constitutional claim asserted here goes well beyond the contours of this case. Recognition of the claim would make it difficult, if not im-

possible, for Congress and the Commissioner to enforce the safety and efficacy requirements of the Act with respect to any drug that a court might conclude is nontoxic, that a physician somewhere is willing to prescribe, and that some individual wishes to take. And recognition of the constitutional claim would impede the states as well as the federal government from enforcing health-related regulation of drugs.

3. Even if the constitutional right of privacy did include a right to take particular drugs for medical purposes, any such right to use Laetrile is outweighed by compelling governmental interests in protecting the public health.

Specifically, the government has a compelling interest (1) in maintaining the confidence of the public and the medical profession in the safety and efficacy of the marketed drug supply; (2) in seeing that persons suffering from cancer, both in its early and later stages, are not deterred by the availability of an unproven drug such as Laetrile from seeking timely treatment by therapies of proven effectiveness; and (3) in seeing that cancer patients and their families are not defrauded by the promotion of costly but ineffective drugs.

Prohibiting the importation and interstate distribution of Laetrile is a reasonable means of effectuating these interests—even where only the availability of Laetrile to patients classified as “terminally ill” is concerned, and even assuming that patients in this class are beyond the help of conventional therapies. Government acquiescence in even limited avail-

ability of Laetrile may suggest to cancer patients generally that the drug has some value. There is a real danger, illustrated by incidents of record in this case, that drugs ostensibly provided for those classified as terminally ill will be made available to other patients whose cancers are demonstrably in earlier, curable stages.

## ARGUMENT

### I

#### THE SAFETY AND EFFECTIVENESS REQUIREMENTS OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT APPLY TO DRUGS INTENDED FOR USE BY THE TERMINALLY ILL

The court of appeals cited no authority of any kind for its conclusion that the safety and effectiveness requirements of the Federal Food, Drug, and Cosmetic Act do not apply to Laetrile when it is obtained for intravenous administration by physicians to “terminally ill” cancer patients.<sup>13</sup> The court’s conclusion is contrary to the language of the Act, the legislative purpose it embodies, and the consistent and reasonable interpretation placed on the Act by the agency charged with enforcing it. The conclusion is also unsupported by case law or other authority.

<sup>13</sup> We use the term “terminally ill” because that is the term used by the court of appeals to describe the group of patients entitled under its order to use Laetrile despite the drug’s non-compliance with the safety and effectiveness requirements of the Act. However, we are not certain of the meaning of the term, since the court did not define it, and as we note below (page 30), there is no reliable means of identifying such a group.

A. We start with some familiar principles. When the purpose of a congressional enactment "has been effected by plain and unambiguous language, and the act is within the power of Congress, the only duty of the courts is to give it effect according to its terms." *United States v. Lexington Mill Co.*, 232 U.S. 399, 409 (1914); see *TVA v. Hill*, 437 U.S. 153, 173, 187, 193-195 (1978). The only circumstance in which a statute may properly be construed to mean something other than what it plainly says is where a literal reading "would lead to absurd results \* \* \* or would thwart the obvious purpose of the statute." *Trans Alaska Pipeline Rate Case*, 436 U.S. 631, 643 (1978), quoting *Commissioner v. Brown*, 380 U.S. 563, 571 (1965). In particular, implied exceptions to clearly delineated statutory coverage are disfavored and will not be found unless they are essential to avoiding an obvious inconsistency with the statutory scheme. *United States v. Key*, 397 U.S. 322, 324-325 (1970); see *TVA v. Hill*, *supra*, 437 U.S. at 188; 2A *Sutherland on Statutes and Statutory Construction* § 47.11 at 90 (4th ed. C. Sands 1973).

When the proper construction of a statute is in doubt, there is a special principle applicable to legislation such as food and drug laws. It is "the well-accepted principle that remedial legislation such as the Food, Drug, and Cosmetic Act is to be given a liberal construction consistent with the Act's overriding purpose to protect the public health \* \* \*." *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969). But there is no need to invoke

that principle when the "overriding purpose" of protecting the public health can be achieved simply by giving effect to the statute according to its plain terms. *United States v. Lexington Mill Co.*, *supra*, 232 U.S. at 409.

In determining a statute's purpose, courts properly look not only to the language and the legislative history of the Act, but also to the views of the agency charged with administering the Act. *Bayside Enterprises, Inc. v. NLRB*, 429 U.S. 298, 304 (1977); *Red Lion Broadcasting Co. v. FCC*, 395 U.S. 367, 381 (1969); *Udall v. Tallman*, 380 U.S. 1, 16 (1965). Those views are entitled to special weight when Congress, in amending the Act, has declined to alter it so as to defeat the administrative construction. *Red Lion Broadcasting Co. v. FCC*, *supra*, 395 U.S. at 381; *Zemel v. Rusk*, 381 U.S. 1, 11-12 (1965).

B. Here, the statutory language is clear. It provides (Section 505(a) of the Act, 21 U.S.C. 355(a)) that

No person shall introduce or deliver for introduction into interstate commerce any new drug  
\* \* \*

unless a new drug application is effective for that drug; and it defines "new drug" (Section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1)) as

[a]ny drug \* \* \* not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling \* \* \*.



The statute further provides that before a new drug application is approved, the drug must be proved to be safe and effective. It must be proved safe through "adequate tests by all methods reasonably applicable," and it must be proved effective by "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved \* \* \*" (Section 505(d) of the Act, 21 U.S.C. 355(d)).

The statute does provide certain exemptions from these premarketing clearance procedures. Three categories of drugs are exempted: (1) grandfathered drugs; (2) drugs that are not "new"—i.e., that experts generally recognize as safe and effective on the basis of scientific investigations meeting the requirements of Section 505(d) (see *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 629-630 (1973)); and (3) drugs that are intended solely for investigational use by qualified investigators and that meet other requirements specified in regulations authorized by the Act (Section 505(i), 21 U.S.C. 355(i)).

But these exemptions are specific and limited. The Act provides no exemption for drugs intended for the "terminally ill" or for any other group of patients. The language by which Congress has required that drugs be safe and effective before they may be distributed in interstate commerce is inclusive.

To give effect to the Act as written would in no respect offend the congressional purpose. There is no

indication from any source that Congress did not intend to protect the public health by ensuring, as the language of the Act requires, that all available and nonexempt drugs are both safe and effective for their intended uses. On the contrary, the legislative history of both the 1938 Act and the 1962 amendments indicates that Congress intended to make the safety and effectiveness requirements applicable to drugs intended for use by the terminally ill in particular.

In its deliberations preceding enactment of the 1938 Act, in which the preclearance requirement of establishing the safety of new drugs was imposed, Congress expressed its concern over drugs purporting to treat cancer. See, e.g., 79 Cong. Rec. 5023 (1935) (remarks of Sen. Copeland, sponsor of the Act); 83 Cong. Rec. 7786-7787, 7789 (1938) (remarks of Reps. Phillips and Lea). See also S. 2000, 73d Cong., 2d Sess. § 9(c) (1934), reprinted in C. Dunn, *Federal Food, Drug and Cosmetic Act* 58 (1938); S. 5, 75th Cong., 1st Sess. § 3(4) (1937), reprinted in Dunn, *supra*, at 639. And there was no suggestion that cancer drugs would be subject to the Act only when they were to be administered to patients whose cancers were "curable."

During the proceedings leading to the 1962 amendments, Congress recognized that the Act would apply to experimental drugs used to treat "cancer in its last stages." 108 Cong. Rec. 17399 (1962) (remarks of Sen. Kefauver, chairman of the committee reporting the bill). Senator Eastland, another proponent of the bill, assumed that drugs administered for

"fatal diseases, such as cancer," would be subject to the Act's requirements, noting that approval of such drugs would be appropriate even though they might only prolong life or alleviate suffering. 108 Cong. Rec. 17401 (1962).

In accord with the statutory language and the evident congressional purpose, the FDA, in enforcing the safety requirements in Section 505(d) of the Act before 1962 and in enforcing both the safety and the effectiveness requirements since 1962, has never made an exception for new drugs that are to be administered to the terminally ill. Had Congress disapproved of this consistent course of administrative action, it could have amended the Act accordingly when it enacted the 1962 amendments or at any time since.<sup>14</sup>

Nor is there support in the case law for the construction given the Act by the court of appeals here. The only prior federal appellate decision<sup>15</sup> that considered the interests of the terminally ill in obtaining access to an anticancer drug was *Rutherford v.*

<sup>14</sup> In enacting the 1962 amendments, which adopted the effectiveness requirement for all new drugs, Congress specifically approved the FDA's longstanding policy of requiring a demonstration of effectiveness as part of the safety requirement for drugs used in the treatment of life-threatening diseases. S. Rep. No. 1744 (Part 1), 87th Cong., 2d Sess. 15 (1962); H.R. Rep. No. 2464, 87th Cong., 2d Sess. 3 (1962). See pages 47-48, *infra*.

<sup>15</sup> Some district courts have granted preliminary relief permitting cancer patients diagnosed as terminally ill to receive supplies of Laetrile through interstate commerce (see page 50, note 35, *infra*), but none has held the Act's safety and effectiveness standards inapplicable to drugs for the terminally ill.

*American Medical Association*, 379 F.2d 641 (7th Cir. 1967), cert. denied, 389 U.S. 1043 (1968). The court of appeals there implicitly accepted the proposition that the safety and efficacy requirements of the Act apply to drugs intended for use by the terminally ill.<sup>16</sup>

C. The court of appeals ruled that the Act's standards of safety and effectiveness have "no meaning," and hence "no application," with respect to a drug intended for use by cancer patients who are "terminally ill" (Pet. App. 5a-7a). This ruling is erroneous for several reasons.

1. First, and most fundamental, the court substituted its view for that of Congress with respect to what constitutes a reasonable and appropriate regulatory scheme. Where the congressional scheme requires proof of the safety and effectiveness of all new drugs, except those categories of drugs that Congress expressly exempted, the court created a new exemption for drugs intended for a category of patients. It is not for a court to add exemptions to those that Con-

<sup>16</sup> In that case a doctor and "hopeless" cancer patients (379 F.2d at 642) sought to enjoin the FDA and others from interfering with the distribution of another drug allegedly effective in the treatment of cancer. The court held that "initial approval or exemption of a drug is within the primary jurisdiction of the FDA." *Id.* at 643. In the absence of a good faith application to the agency for such approval or exemption, the court lacked jurisdiction to review the refusal to permit the marketing of the drug. *Ibid.* The opinion notes that Section 355 of the Act establishes a procedure for submitting adequate scientific information about a new drug to the FDA to "permit an intelligent assessment of its safety and efficacy" (*ibid.*).

gres provided (*TVA v. Hill*, *supra*, 437 U.S. at 188), or to let its own "individual appraisal of the wisdom or unwisdom of a particular course consciously selected by the Congress" be its guide in interpreting a statute (*id.* at 194).

2. In creating the exception for the "terminally ill"—a term it made no attempt to define—the court of appeals also disregarded the judgment of the Commissioner, supported by expert medical testimony, that there is no objectively identifiable group of cancer patients comprising such a class, except in retrospect (Pet. App. 98a, 267a-268a). Cancer in individuals frequently takes an unpredictable course; there may be unexpected and unexplainable remissions, and one person may differ from another in his response to a particular mode of therapy (Pet. App. 98a, 268a). As the Commissioner also found, again with the support of expert testimony, even if one could reliably distinguish between the terminally ill and those who will respond to conventional cancer treatment, it would be virtually impossible, as a practical matter, to restrict the use of Laetrile to the terminally ill (Pet. App. 269a-270a).

Judgments such as these, reflecting an agency's technical expertise supported by substantial record evidence, may not simply be disregarded by the courts. *Ciba Corp. v. Weinberger*, 412 U.S. 640, 643-644 (1973); *United States v. An Article of Drug . . . Bacto-Unidisk*, *supra*, 394 U.S. at 791-792; *New York v. United States*, 331 U.S. 284, 327 (1947). See also *Vermont Yankee Nuclear Power Corp. v.*

*Natural Resources Defense Council, Inc.*, 435 U.S. 519, 557-558 (1978).

3. Even if it were appropriate for a court to depart from the plain meaning of legislation and the record-supported judgment of the expert agency in order to avoid "unreasonable" results, the decision of the court of appeals would be improper because there is no unreasonable result to avoid. There is nothing unreasonable in protecting patients diagnosed as "terminally ill" from unsafe or ineffective drugs, and the court was wrong in thinking that the Act's standards of safety and effectiveness have no meaningful application to drugs intended for use by such patients.<sup>17</sup>

A drug is "safe," within the meaning of the Act, if the benefits expected to be achieved through its administration outweigh the costs or risks incurred.<sup>18</sup>

<sup>17</sup> We assume *arguendo* at this point that the "terminally ill" can be reliably identified. In fact, as we have noted, they cannot be, and any class of patients so certified may be expected to include some for whom conventional therapies may succeed, at least in significantly prolonging life. The Act's standards of safety and effectiveness are surely applicable to such patients, even if one accepts the view of the court of appeals that they are not applicable to patients whose illness is truly "terminal."

<sup>18</sup> "[A] drug is safe when the expected therapeutic gain justifies the risk entailed in using it \* \* \*." Dr. Theodore G. Klumpp, Chief, Drug Division, FDA, June 23, 1941, Food Drug Cos. L. Rep. (CCH) ¶ 71,053.59, at 71,063; see also M. White, "Administrative Procedure and Practice in the Department of Agriculture under the Federal Food, Drug, and Cosmetic Act of 1938" 95 (1940), reprinted in H. Toulmin, Jr., *A Treatise on the Law of Food, Drugs and Cosmetics* 635 (1942).



No drug is completely "safe" in the lay person's sense of the word, since every drug—aspirin not excepted—involves risks.<sup>19</sup> Thus, safety has the same meaning with respect to drugs intended for terminally ill cancer patients as it does generally. A drug that may shorten a terminally ill patient's life expectancy or cause other physical harm, without a more-than-compensating potential for benefiting the patient, is unsafe. The judgment of the court of appeals, limiting its authorized use of Laetrile by requiring that the drug be administered only by a licensed physician and only through intravenous injection (Pet. App. 8a-9a), betrays the court's own recognition that considerations of safety are applicable to regulation of the use of drugs by the terminally ill.<sup>20</sup>

"Effectiveness" under the Act requires the sponsor of a drug to provide substantial evidence that the drug produces the effects claimed for it. Section 505 (d), 21 U.S.C. 355(d).<sup>21</sup> Effectiveness does not, as

<sup>19</sup> See L. Goodman & A. Gilman, *The Pharmacological Basis of Therapeutics* 325-339 (5th ed. 1975).

<sup>20</sup> The Act itself distinguishes between drugs that are safe for self-administration and those that are safe only when administered by a physician. See, e.g., Section 503(b) of the Act, 21 U.S.C. 353(b). The court's restriction on the method of administration (and its denial of respondents' petition requesting an amendment of the judgment to permit the use of Laetrile in oral form) is unexplained, but may reflect the court's acknowledgement of record evidence indicating that Laetrile taken orally is toxic (Pet. App. 157a-162a).

<sup>21</sup> There is a relationship, of course, between drug safety and efficacy. As Senator Kefauver stated when introducing the bill that became the 1962 amendments, "[a]n otherwise

the court of appeals implied (Pet. App. 6a), necessarily connote curative properties.<sup>22</sup> Thus, for a terminally ill patient, as for anyone else, a drug that fails, by objective measures, to fulfill its sponsor's claim of increased life expectancy, ameliorated physical condition, or reduced pain is ineffective.

The terminally ill, whether victims of cancer or of any other disease, have as much interest as the general public in protection from drugs that are not both safe and effective. To exempt Laetrile from the Act's requirements when used by terminally ill cancer patients would, as the Commissioner concluded (Pet. App. 270a):

\* \* \* lead to needless deaths and suffering among (1) patients characterized as "terminal" who could actually be helped by legitimate therapy and (2) patients clearly susceptible to the benefits of legitimate therapy who would be misled as to Laetrile's utility by the limited approval program or who would be able to obtain the drug through the inevitable leakage in any system set up to administer such a program.

Moreover, as the Commissioner noted (Pet. App. 224a-230a), the vulnerable psychological state of can-

completely safe drug can be dangerous to the patient if it does not have the therapeutic effect in use which it is represented to have." 107 Cong. Rec. 5640 (1961).

<sup>22</sup> Neither does it involve consideration of the relative effectiveness of one drug compared with another, or require proof of unanimous scientific opinion. S.Rep. No. 1744 (Part 1), 87th Cong., 2d Sess. 56-58 (1962) (views of Sen. Dirksen and Sen. Hruska); S. Rep. No. 1744 (Part 2), 87th Cong., 2d Sess. 6 (1962).

cer patients may make them particularly susceptible to unfounded claims and thus create a special need for protection from ineffective drugs.<sup>23</sup>

D. In sum, the decision of the court of appeals represents an improper substitution of its own judgment for that of Congress and the Commissioner, who have determined that an exemption from the Act's safety and effectiveness requirements for drugs used by cancer patients characterized as "terminally ill" is neither appropriate nor feasible. The court's decision seriously limits the Commissioner's power to protect the public from unsafe and ineffective drugs.

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<sup>23</sup> If the decision of the court of appeals was animated by an unarticulated view that Laetrile may be the only hope available for terminally ill cancer patients who are not aided by conventional therapy, that view was misconceived. Many different experimental cancer drugs are available. Under Section 505(i) of the Act, 21 U.S.C. 355(i), exemptions from the premarketing requirements of Section 505(d) may be given for drugs intended solely for investigational use, if pre-clinical tests of the drug (including tests on animals) are "adequate to justify the proposed clinical testing" and if certain other requirements as to recordkeeping and informed consent are met. FDA records show that at the present time there are more than 300 oncologic drugs under clinical investigation under exemptions granted pursuant to 21 U.S.C. 355(i). All of these drugs are available, at authorized institutions, for use by critically ill patients.

We are informed by the National Cancer Institute (NCI) that during 1977 some 63,000 patients were receiving such drugs in NCI treatment programs or were being evaluated in follow-up programs conducted by NCI's extramural clinical trials division. NCI also reports that in 1977 approximately 12,000 cancer patients were in similar Veterans Administration treatment or follow-up programs. The same year another 22,800 cancer patients were treated with investiga-

Although the present ruling is limited to the intravenous use of Laetrile by terminally ill cancer patients, the court's analysis of the Act would prevent the Commissioner from concluding that any drug intended for use by the terminally ill has not been shown to be safe and effective. See Comment, *Laetrile: Statutory and Constitutional Limitations on the Regulation of Ineffective Drugs*, 127 U. Pa. L. Rev. 233, 255 (1978). The decision thus would make it difficult, if not impossible, for the Commissioner to discharge his statutory responsibility to keep unproven drugs out of the marketplace.<sup>24</sup>

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tional drugs in programs directed by independent investigators under NCI auspices. In addition to conducting clinical trials on promising drugs, NCI screens from 15,000 to 30,000 natural and synthetic compounds a year to determine their potential anti-cancer activity; between 1956 and 1976, over 475,000 compounds were evaluated. See Division of Cancer Treatment, National Cancer Institute, *Treatment Linear Assay* 3 (December 1976).

An application by NCI to undertake clinical testing of Laetrile is pending before the Commissioner.

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<sup>24</sup> The court directed the FDA to "promulgate regulations \* \* \* as if the drug was found by the Commission[er] to be 'safe' and 'effective' for the limited group of persons here considered" (Pet. App. 7a). It is difficult to see how the FDA could comply. In the absence of adequate data, there is no basis on which to label Laetrile in the manner required by Section 502 (21 U.S.C. 352). Directions for drug use—including indications, contraindications, dosages, routes of administration, warnings, side effects, and necessary collateral measures—are premised on a body of data derived from extensive testing. As the Commissioner found, such data do not exist for Laetrile (Pet. App. 93a-211a, 270a-272a); neither court below disagreed with this conclusion. Without such testing data, the drug cannot be labeled for any use. Any

## II

LAETRILE IS A NEW DRUG THAT IS NOT EXEMPTED FROM THE PREMARKETING CLEARANCE REQUIREMENTS OF THE ACT BY OPERATION OF THE 1962 GRANDFATHER CLAUSE

1. The Commission found (a) that Laetrile is a new drug subject to the premarketing clearance requirements of the Act because it is not generally recognized by qualified experts as safe and effective (Pet. App. 88a-162a), and (b) that Laetrile does not qualify for exemption under the 1962 grandfather clause because it fails to meet four of the five requirements for such exemption (Pet. App. 179a-211a). The district court sustained the former finding (Pet. App. 22a) but rejected the latter (Pet. App. 25a-27a).<sup>25</sup> In rejecting the Commissioner's grandfather clause determination, the district court

suggestion in labeling that the drug may be safely or effectively used would misbrand the drug in violation of Sections 502(a) and 505(d)(6) (21 U.S.C. 352(a) and 355(d)(6)). Effective regulations authorizing an affidavit system similar to that now maintained by order of the district court (A. 5-6, 57-58) (see page 5, note 6, *supra*) would also be difficult to devise, since there have been indications that the current system results in distribution of Laetrile to persons not within the certified class of terminally ill cancer patients (see page 74, *infra*).

<sup>25</sup> As noted above (page 11), the Commissioner also concluded that Laetrile is not entitled to exemption under the 1938 grandfather clause (included in Section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1)), and the district court did not overturn this conclusion. Respondents did not raise this issue in the court of appeals.

misunderstood the purpose of the clause and improperly reversed the Commissioner's factual findings with regard to the chemical composition of the 1962 drug, its safety reputation among medical experts, its commercial availability, and its labeling.

The 1962 grandfather clause, Pub. L. No. 87-781, Section 107(c)(4), 76 Stat. 789, provides:

In the case of any drug which, on [October 9, 1962] the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective [new drug] application under section 505 of that Act, the amendments to section 201 (p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

The purpose of grandfather clauses generally is to protect the reliance interests of those whose previously lawful investments or means of earning income would be adversely affected by application of new legislation. See, *e.g.*, *New Orleans v. Dukes*, 427 U.S. 297, 305 (1976). The purpose of this grandfather clause is to permit the continued marketing—without compliance with the new effectiveness requirement established by the 1962 amendments—of certain established drugs that were lawfully marketed without an approved new drug application in 1962 because they were generally recognized as safe for



their labeled uses. *USV Pharmaceutical Corp. v. Weinberger*, 412 U.S. 655, 663-664 (1973). Drugs lawfully marketed as "new drugs" in 1962 were not exempted from the effectiveness requirement imposed by the 1962 amendments, but were given a two-year grace period in which to comply. *Ibid.*<sup>26</sup> A fortiori, Congress did not intend by the 1962 grandfather clause to establish criteria that a subsequently introduced product, not marketed in 1962, could meet in order to avoid having to provide the proof of effectiveness required by the 1962 amendments.

Laetrile was not being marketed commercially on October 9, 1962, and has not been continuously marketed in the same composition and with the same labeling since that date. The present proponents of Laetrile, moreover, do not claim that *they* were marketing the drug in 1962.<sup>27</sup> They thus do not seek

<sup>26</sup> Thus, a drug that *was* "covered by an effective [new drug] application" on October 9, 1962, was thereby excluded from the grandfather clause (see subpart (C), quoted at page 37, *supra*); but, under another section of the 1962 amendments (Section 107(c)(3), 76 Stat. 788-789), such a drug was allowed to continue being marketed for two years. This was to give manufacturers of drugs covered by NDA's a reasonable opportunity to generate effectiveness data in order to qualify the drugs for marketing under the new amendments.

<sup>27</sup> Participation in the proceeding before the Commissioner was not limited to the parties to the district court suit and their designated witnesses. All who wished to make oral presentations, written submissions, or both, were permitted to do so, whether or not they had any connection with the court action. (Pet. App. 48a-51a). Those who submitted presentations aimed at supporting the claim that Laetrile should be

protection of interests enjoyed by manufacturers in 1962 and maintained to the present. Rather, they seek to justify an essentially new marketing venture under the mantle of various pre-1962 drugs. Even if their claim to satisfy the requirements of the 1962 grandfather clause were more colorable than it is, it would distort the purpose of the clause to extend its protection to them. It would also offend the principle that such a clause, as a restriction on the scope of remedial legislation and a limitation of the protection afforded the public against ineffective drugs, should be narrowly construed. *USV Pharmaceutical Corp. v. Weinberger*, *supra*, 412 U.S. at 667; *Weinberger v. Hynson, Westcott & Dunning, Inc.*, *supra*, 412 U.S. at 633-634; *Durovic v. Richardson*, 479 F.2d 242, 250 n.6 (7th Cir.), cert. denied, 414 U.S. 944 (1973); *United States v. An Article of Drug . . . "Bentex Ulcerine"*, 469 F.2d 875, 878 (5th Cir. 1972), cert. denied, 412 U.S. 938 (1973).

2. Although the 1962 grandfather clause has three subparts designated (A), (B), and (C), it essentially sets out, as noted above (page 11-12, *supra*), five factual propositions that must be established as the

available for distribution through interstate commerce included cancer patients (Pet. App. 231a, 235a), persons associated with the development of Laetrile as a drug recommended for the treatment of cancer (Pet. App. 50a, 79a-88a), and persons who dispense the drug through clinics (Pet. App. 237a). The Commissioner considered all views submitted for the record (Pet. App. 50a-51a). Hence our references to "proponents" of Laetrile are not limited to respondents and their witnesses and representatives.

basis for exempting a drug from the effectiveness requirements imposed by the 1962 amendments. Failure to prove any one of the five makes the exemption inapplicable. *United States v. An Article of Drug . . . "Bentex Ulcerine," supra*, 469 F.2d at 878. Thus the proponents of Laetrile had the burden of proving: (1) that present-day Laetrile is chemically identical to a drug in existence on October 9, 1962; (2) that the drug was then commercially available; (3) that the drug was at that time generally recognized by experts as safe for its intended use (and thus was not a "new drug" under the 1938 Act); (4) that present labeling (including directions for use) is the same as the labeling on the drug as sold on October 9, 1962; and (5) that the drug was not then covered by an effective NDA under the 1938 Act.

The Commissioner found that the proponents of Laetrile had failed to meet all but the last of these requirements and that Laetrile therefore is not exempt under the 1962 grandfather clause. The district court reached a contrary conclusion by reweighing the scientific evidence and substituting its own findings for those of the Commissioner; the court did not determine, under the appropriate standard of judicial review of administrative findings, that the Commissioner's decision was arbitrary and capricious or was not supported by substantial evidence. See *Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 413-414 (1971); *Illinois Central R.R. v. Norfolk & Western Ry.*, 385 U.S. 57, 65-66 (1966); *Consolo v. FMC*, 383 U.S. 607, 618-620 (1966).

a. *Composition*. First, the Commissioner properly found that the proponents of Laetrile had failed to demonstrate that the drug or drugs now sold as Laetrile have the same composition as a drug sold on October 9, 1962. As the Commissioner noted, the fact that a drug used or sold on October 9, 1962, has some ingredients in common with a drug used or sold today would not establish identity of composition sufficient to satisfy the requirements of the grandfather clause (Pet. App. 182a-183a). A change in any of the ingredients, including inactive ingredients, or in the proportion of the ingredients, will make a drug a "new drug." See 21 C.F.R. 310.3(h); *United States v. An Article of Drug . . . "Entrol-C Medicated,"* 513 F.2d 1127, 1130 n.7 (9th Cir. 1975).

The Commissioner found that the composition of the different substances referred to as Laetrile both before and after 1962 varied considerably, and that the 1962 formulations differed from the formulations currently in use (Pet. App. 182a-187a).<sup>28</sup> Consequently, he determined that the proponents of Laetrile had failed to sustain the burden of showing that either Laetrile or amygdalin as presently constituted was in use on October 9, 1962. *Ibid*.

The district court rejected the Commissioner's findings on this point and found "that Laetrile and Amygdalin are equivalent and have been recognized

<sup>28</sup> Laboratory analyses of drugs called Laetrile have often revealed both variances from labeled composition and variations in component parts and in the percentage of amygdalin present (Pet. App. 184a-185a).

as such for over 20 years" (Pet. App. 26a n. 17).<sup>30</sup> The court did not identify the quantitative or qualitative composition of any drug sold on October 9, 1962, but relied instead on general references in the record to an identity between Laetrile and amygdalin, none of which was specific as to chemical formulation for any given date.<sup>30</sup> Even if the references cited by the court supported its conclusion, they would not provide an adequate basis for displacing the Commissioner's finding that Laetrile in its present forms was not in use on October 9, 1962,

<sup>30</sup> This conclusion is contrary to that reached by the district court in *United States v. Earthco*, No. CV 78-3602-HP (C.D. Cal. Jan. 24, 1979).

<sup>30</sup> None of the materials cited by the district court (Pet. App. 26a n.17) comes close to establishing the identity of any of the current Laetrile formulations with any drug available in 1962 or before. For example, the court cited and quoted the Commissioner's statement that "Laetrile is the name of a product whose major component or ingredient is the chemical amygdalin, \* \* \*" (emphasis supplied). It also cited (*ibid.*) a pamphlet prepared by the American Cancer Society for distribution to the public, a document that can hardly be expected to provide precise information on the formulation of the drug. Frank Rauscher's "Statement Concerning Laetrile" (A. 59-60), contrary to the court's assertion (Pet. App. 26a n.17), does not even mention "amygdalin." Neither the deposition of Dean Burk (A. 67-76), which uses the terms "Laetrile" and "amygdalin" interchangeably, nor the deposition of Raymond Ewell (A. 77-79), attempts to identify a formulation for Laetrile or amygdalin at any specific time. All that Dr. Ewell stated was that "only a few people consume amygdalin in its pure form," which is "known popularly as laetrile." Other record references by the district court are similarly irrelevant to the issue of chemical identity.

since the Commissioner's finding is based on substantial evidence of record and is not arbitrary or capricious (Pet. App. 187a). See, e.g., *Citizens to Preserve Overton Park v. Volpe*, *supra*, 401 U.S. at 413-414.

b. *Commercial availability.* The district court committed similar error in rejecting the Commissioner's findings on the commercial availability of Laetrile on October 9, 1962. Commercial availability means that the drug has been "openly and readily available and broadly distributed in the ordinary course of business" and that there was no "restriction to investigational use \* \* \*." *Durovic v. Richardson*, *supra*, 479 F.2d at 248. Unless a drug was available generally for commercial use on October 9, 1962, the manufacturer lacks the reliance interest recognized by Congress as warranting an exception to the requirement of effectiveness. The administrative record fully supports the Commissioner's conclusions that Laetrile, as of October 9, 1962, was not openly and readily available and was not broadly distributed in the ordinary course of business, but was in fact restricted to investigational use (Pet. App. 187a-190a).<sup>31</sup>

<sup>31</sup> As the Commissioner noted, Dr. Ernst T. Krebs, Sr., a developer of Laetrile, stated in a 1965 affidavit that his shipments of Laetrile from as early as 1926 and up through 1962 "were for investigational use only" (Pet. App. 187a). The conclusion that the use of Laetrile was continuously investigational in nature was reinforced by other evidence. First, in 1952, the FDA collected Laetrile labeling which read in part: "Caution: New drug limited by Federal Law to investigational use" (Pet. App. 189a). Second, on October 3, 1962,



The district court recognized, as did the Commissioner, that investigational use of a drug does not prove commercial availability, and it attempted to rely on other evidence from the record (Pet. App. 29a & n.21). Although the court's opinion states that "[t]he record's whole tenor reasonably establishes the commercial availability of Laetrile (Amygdalin) during the period in question" (Pet. App. 30a n.21), only two submissions are cited. One is an affidavit by Charles Gurchot, Ph.D., which stated that amygdalin was "a purchaseable item in various chemical catalogs published in the United States" (*ibid.*). The other is a letter from N. Schneider of Van, Waters & Rogers, Inc., a chemical supply house dealing in amygdalin (*ibid.*), which simply quoted prices for amygdalin; it did not provide chemical specifications.

Even if it is assumed, contrary to the Commissioner's finding, that present-day Laetrile and amygdalin are chemically identical substances, proof that a chemical supply house was selling the compound amygdalin before 1962 does not establish that a drug with that chemical composition was then com-

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Ernst T. Krebs, Jr., submitted an NDA for Laetrile (Pet. App. 191a-192a) (describing the drug as approximately 80% amygdalin, *id.* at 185a); since at that time the Act defined a "new drug" as one not generally recognized as safe, the filing of the NDA constituted an acknowledgement by one of its leading proponents that Laetrile was not generally recognized as safe and was restricted to investigational use (see Pet. App. 181a). Third, under the terms of his probation following conviction for selling another unproven drug, Ernst Krebs, Jr., was permitted by court order on June 28, 1962, to ship some Laetrile in interstate commerce for investigational use only (Pet. App. 187a-188a).

mercially available. A chemical supply house sells raw chemicals, not pharmaceuticals prepared in dosage forms with labeling for use as drugs. Such a firm would lack a cognizable proprietary interest in the sale of a drug, and there would thus be no reason to permit the firm itself—let alone others having no connection with it—to sell such compounds as drugs after October 9, 1962, without meeting the new standards of the Act.

c. *Safety.* The 1962 grandfather clause, by its exclusion of drugs that were "new drugs" as defined in Section 201(p) of the pre-existing Act, requires a drug to have been generally recognized as safe under its labeled conditions of use on October 9, 1962.<sup>32</sup> This, in turn, signifies that there must have existed on October 9, 1962, "investigations \* \* \* includ[ing] adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use \* \* \*." Section 505(d)(1) of the Act, 21 U.S.C. 355(d)(1); *Weinberger v. Bentex Pharmaceuticals, Inc.*, 412 U.S. 645, 653 (1973) ("the reach of scientific inquiry under both § 505(d) and under § 201(p) is precisely the same"). Unless data from such tests were available in the scientific literature, there could be no basis for general recognition of safety among experts. *Weinberger v. Hynson, Westcott & Dunning, Inc.*, *supra*; see also, e.g., *United States v. 41 Cases, More or Less*, 420 F.2d 1126, 1130 (5th Cir. 1970).

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<sup>32</sup> Section 201(p), 21 U.S.C. (1958 ed.) 321(p), as it appeared prior to the 1962 amendment, appears at Pet. App. 180a.

The administrative record fully documents the absence in 1962, and today, of any general recognition among qualified experts of Laetrile's safety. Indeed, the record contains substantial evidence (see Pet. App. 201a-208a) indicating that Laetrile was not generally known at all to the community of medical experts on October 9, 1962. Moreover, as noted earlier, because of the pre-1962 variability in the composition of Laetrile, and the varied conditions of use recommended in its labeling, Laetrile could in no event have been generally recognized as a drug whose composition was safe "for use under the conditions prescribed, recommended, or suggested in the labeling" for it. 21 U.S.C. (1958 ed.) 321(p)(1) (Pet. App. 180a).

The Commissioner's finding that Laetrile was not generally recognized by experts as safe on October 9, 1962, did not rest solely on the absence of scientifically developed data indicative of the drug's safety. It was also based on testimony of some of the nation's leading cancer scientists that Laetrile presents significant hazards to persons to whom it is administered (Pet. App. 158a-160a, 162a). For example, Dr. Joseph F. Ross, professor of medicine and Director of the Research Training Program in Hematology and Hematologic Oncology at UCLA (Pet. App. 146a), testified that oral ingestion of Laetrile or amygdalin presents "a definite health hazard" because it "may produce acute cyanide poisoning" (Pet. App. 162a). Even proponents of Laetrile have labeled the drug to warn of the toxic effects of oral administration (Pet. App. 158a).

In determining that Laetrile was generally recognized as safe on October 9, 1962 (Pet. App. 33a), the district court did not address the implications of the lack of any scientific data on the safety of Laetrile on or prior to that date.<sup>33</sup> Instead, contrary to this Court's decisions (*e.g.*, *Weinberger v. Hynson, Westcott & Dunning, Inc.*, *supra*), the district court relied on anecdotal experiences recounted in several submissions from Laetrile proponents (Pet. App. 33a n.24).

The district court compounded this error by holding that no showing of Laetrile's effectiveness as a cancer drug was required in order for it to have been generally recognized as safe on October 9, 1962 (Pet. App. 28a n.18). Congress, when it was considering the 1962 amendments to the Act, recognized that in the case of drugs used for life-threatening diseases, evidence of effectiveness was considered by the FDA to be essential to proof of safety. The Senate Report on the 1962 amendments stated:

The Food and Drug Administration now requires, in determining whether a "new drug" is safe, a showing as to the drug's effectiveness where the drug is offered for use in the treatment of a life-threatening disease, or where it appears that the "new drug" will occasionally

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<sup>33</sup> The district court did not make any specific findings on this point and cited only a single record reference—which the Commissioner found reasons to discount (Pet. App. 206a-207a)—indicating an affiant's information and belief that "pure amygdalin" has been generally recognized as safe among qualified experts since the 1930's (Pet. App. 33a n.24).

produce serious toxic or even lethal effects so that only its usefulness would justify the risks involved in its use.

S. Rep. No. 1744 (Part 1), 87th Cong., 2d Sess. 15 (1962). The legislative reports make it clear that the amendments were not intended to affect the then-existing authority of the FDA to pursue this practice of considering the effectiveness of a new drug to be used for a life-threatening disease in the context of passing on its safety. *Ibid.*; see also H.R. Rep. No. 2464, 87th Cong., 2d Sess. 3 (1962). Thus, a lack of general recognition of the effectiveness of a drug intended for treatment of a life-threatening disease on October 9, 1962, means that general recognition of its safety could not have existed. As the Seventh Circuit held in *Durovic v. Richardson*, *supra*, 479 F.2d at 250: "a drug offered for use in the treatment of cancer is now, and was before the amendments, a new drug unless it has achieved general recognition among the experts as safe and effective for such use."

The record discloses that there was no general recognition of Laetrile's effectiveness on October 9, 1962 (Pet. App. 100a-154a, 208a-211a), and the district court indeed upheld the Commissioner's finding to that effect (Pet. App. 22a). Thus, as a drug offered for use in the treatment of a life-threatening disease, Laetrile could not meet the 1962 grandfather clause requirement of achieving general recognition of safety because it had not achieved general recognition of effectiveness. This consideration rein-

forces the Commissioner's conclusion based on the evidence concerning safety itself.

d. *Labeling*. To show that Laetrile labeling existed in 1962, the district court relied solely on the affidavit of Robert S. K. Young, M.D., Ph.D., which stated that 1962 labeling had characterized Laetrile as a palliative agent for use in "cancers beyond aid by standard agents" and had warned that "it is not to be employed to the exclusion of surgery, radiation or similar standard modalities so long as they are indicated" (Pet. App. 15a n.7; A. 63). What the district court did not note is that Dr. Young's affidavit referred to labeling that was proposed for Laetrile as a drug in investigational use. This was the labeling included in the NDA submitted by Ernst Krebs, Jr., on October 3, 1962 (see Pet. App. 191a-192a). This labeling thus was not for a product commercially sold or used on October 9, 1962. Moreover, Dr. Young stated that, in fact, the 1962 proposed labeling differed significantly from 1965 labeling in FDA's possession (A. 63-66).

The Commissioner's finding that "Laetrile as now known is not intended solely for use under conditions recommended in labeling on October 9, 1962" (Pet. App. 199a) is supported by substantial record evidence (Pet. App. 191a-199a). This included evidence that, in contrast to the labeling suggested by Ernst Krebs, Jr., on October 3, 1962, Laetrile was described after 1962 as a therapy that could, and should, be used to the exclusion of other cancer therapies (Pet. App. 196a-197a). There was also



evidence that oral administration of Laetrile first appeared after 1962 (Pet. App. 194a-195a, 198a, and that suggested dosages have ranged from 1.5 grams to more than 9 grams, with no scientific rationale to account for the differing recommendations (Pet. App. 192a, 196a).<sup>34</sup> The district court's reversal of the Commissioner's finding was erroneous.

3. In sum, the Commissioner, supported by substantial evidence of record, concluded that Laetrile failed to satisfy four separate and necessary conditions for grandfather status under the 1962 amendments. This conclusion is in accord with the decisions of all federal courts that have considered the issue, with the exception of the district court below and a few district courts that have relied on the decisions below in granting preliminary relief.<sup>35</sup> With

<sup>34</sup> Indeed, the record indicates an absence of any uniform standard or generally recognized labeling either before or after 1962. For example, pre-1962 labeling varied widely with respect to the proper method of administration; suggested methods included injection into muscles and "iontophoresis," a method—which the Commissioner termed "bizarre" (Pet. App. 193a)—employing galvanic current to force Laetrile into the cancer cells (Pet. App. 193a-194a).

<sup>35</sup> Subsequent to the district court's initial decision (A. 20-30), similar actions were instituted by cancer patients in other courts. In *Carnohan v. United States*, No. 77-0010 (S.D. Cal. Jan. 6, 1977), and *Rizzo v. United States*, 432 F. Supp. 356 (E.D. N.Y. 1977), the district courts, relying on the initial decision of the court of appeals below (A. 31-41), granted preliminary injunctions allowing plaintiffs to transport Laetrile in interstate commerce. Both cases were dismissed upon the death of the plaintiffs. Three other cases were dismissed after temporary restraining orders were granted. See, e.g., *Keene v. United States*, No. 76-0249 (S.D. W.Va., dismissed Sept. 28, 1976).

those exceptions, the federal decisions concerning Laetrile (or related drugs under other names) have held that it is a new drug fully subject to the statutory requirements that safety and effectiveness be shown by scientific evidence, or have concluded on requests for preliminary relief that the likelihood of success on that issue lies with the government. See, e.g., *United States v. Mosinee Research Corp.*, 583 F.2d 930, 932 (7th Cir. 1978); *United States v. Spectro Foods Corp.*, Civ. No. 76-101 (D. N.J. Jan. 29, 1976), aff'd in pertinent part, 544 F.2d 1175, 1179-1180 (3d Cir. 1976); *Hanson v. United States*, 417 F. Supp. 30, 34-36 (D. Minn. 1976), aff'd, 540 F.2d 947 (8th Cir. 1976); *United States v. Earthco*, No. CV 78-3602-HP (C.D. Cal. Jan. 24, 1979); *Gadler v. United States*, 425 F. Supp. 244, 247-249 (D. Minn. 1977); *In re Morgan v. Matthews*, No. 76-1637 (D. S.C. Nov. 30, 1976); *United States v. General Research Laboratories*, 397 F. Supp. 197, 199 (C.D. Cal. 1975).

In extending grandfather protection to Laetrile, which was not an established anti-cancer drug generally recognized by experts as safe prior to October 9, 1962, the district court disregarded the teaching of this Court that liberality in the construction of the Act does not justify carving out exemptions, but "more appropriately belongs to enforcement of the central purpose of the Act" (*United States v. Dotterweich*, 320 U.S. 277, 284 (1943)). The district court applied an improper standard of review to the Commissioner's factual findings on all four of the points

at issue, and erred in failing to sustain those findings. Thus the district court's holding that Laetrile is exempt under the 1962 grandfather clause provides no basis for affirming the judgment of the court of appeals.

### III

#### NO CONSTITUTIONAL RIGHT OF PRIVACY ENJOYED BY TERMINALLY ILL CANCER PATIENTS OR ANYONE ELSE PROTECTS ACCESS TO A DRUG SUCH AS LAETRILE

The district court held that "[b]y denying the right to use a nontoxic substance [Laetrile] in connection with one's own personal health-care, FDA has offended the constitutional right of privacy" (Pet. App. 41a). This holding is erroneous and affords no ground for sustaining the decision of the court of appeals. First, the holding is premised on the court's unwarranted belief, contrary to the well-supported findings of the Commissioner, that Laetrile has been shown to be nontoxic. Second, even if Laetrile were not toxic, there is no constitutional right to take any particular drug or class of drugs for medical purposes. Third, even if the constitutional right of privacy would otherwise include a right to take particular drugs for medical purposes, any such right to use Laetrile is outweighed by a compelling governmental interest in protecting the public health and welfare.

#### A. In Declaring Laetrile to be Nontoxic the District Court Improperly Contradicted the Well-Supported Findings of the Commissioner

The district court's constitutional holding was premised on its view that Laetrile is "nontoxic" and "innocuous" (Pet. App. 38a, 41a). The court stated that "the vast amount of practical experience of actual experimenters and users, in administering Laetrile both parenterally and orally, has established its nontoxicity" (Pet. App. 29a n.18).<sup>36</sup> In so determining, the court contradicted the findings of the Commissioner. As related above (pages 7-9, *supra*), the Commissioner found that Laetrile has not been adequately tested for safety and that it is not generally recognized by experts as safe for use in man (Pet. App. 154a-162a). These findings were based on a review of the scientific literature (Pet. App. 155a-157a) and on the testimony of experts, who testified that the safety of Laetrile has not been demonstrated and that there are definite indications that, at least in its oral form, Laetrile is toxic (Pet. App. 155a-162a, 254a-257a, 271a). The findings were also based on recognition by Laetrile's pro-

<sup>36</sup> The court gave two citations for this statement, neither of which supports it. Footnote 15 of the court's opinion (Pet. App. 24a) discusses the placebo effect of Laetrile, not its safety. Page 311 of the transcript reports the testimony of plaintiff Rutherford, a user of Laetrile and not a scientist, that he uses one 500 milligram tablet "to as high as nine of them in a day's time depending on what this carcass is telling me \* \* \*" (A. 85).

ponents of the possible toxicity of the drug in its oral form (Pet. App. 86a-88a, 158a, 254a-255a).<sup>37</sup>

In rejecting the Commissioner's findings, the district court relied on one laboratory study and the views of Laetrile practitioners (Pet. App. 31a n.23). The laboratory study,<sup>38</sup> though not specifically discussed in the Commissioner's opinion, was impugned as a scientific endeavor by a toxicologist who reviewed it,<sup>39</sup> and the Commission obviously rejected it as sound evidence upon which to conclude that Laetrile is not toxic (Pet. App. 155a-162a). The court's reliance on the casual observations of physicians who

<sup>37</sup> As noted earlier (page 9, note 8, *supra*), reports appearing in the medical literature after the administrative hearing support the toxic nature of oral Laetrile and raise new questions about its toxicity in other forms.

<sup>38</sup> The study was conducted by Harold Manner, Ph.D., a professor of biology (R. 262). ("R." refers to the record in the hearing before the Commissioner.) He injected Laetrile at various doses into mice for 15 days. No mice died as a result, although loss of hair and hyperactivity were observed at higher doses. It appears that Dr. Manner assessed toxicity reactions on the basis of visual examinations and weight gain only. He did not perform drug chemical analyses of animal tissues or fluids. See note 39, *infra*.

<sup>39</sup> The record contains the affidavit of Jacqueline Verrett, Ph.D., a toxicologist, who criticized the Manner data as unscientific and unreliable (R-427): "The authors did not report the performance of any clinical chemical tests (especially cyanohemoglobin determinations), nor the necropsing of the mice or the performance of microscopic study of the tissues. Therefore, it cannot be determined whether there were changes in the chemical status of the mice \* \* \* in the tissues as a result of the administration of amygdalin." She concluded that the study was "inadequate for determining that amygdalin was safe for human consumption."

advocate Laetrile in their practices was equally inappropriate. See *Weinberger v. Hynson, Westcott & Dunning, Inc.*, *supra*, 412 U.S. at 619.<sup>40</sup>

In any event, the court had no warrant to weigh the scientific evidence afresh; it was "hardly qualified to second guess" the scientific judgment of the Commissioner. *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 792 (1969). It was error for the court to ignore the considered opinions of leading cancer specialists on which the Commissioner relied, and to accept instead the anecdotal experiences of a handful of Laetrile practitioners who themselves are not qualified experts. The Commissioner's finding that Laetrile had not been shown to be safe was supported by the evidence and should have been upheld. See *Citizens to Preserve Overton Park v. Volpe*, *supra*, 401 U.S. at 413-414. Thus, the court's constitutional holding, taken on its own

<sup>40</sup> The district court relied on the personal experience of Drs. Binzel, Thompson, McDonald and Nieper. Pet. App. 31a-32a. The qualifications of Drs. Thompson and Nieper are not contained in the record. The Commissioner concluded that Drs. Binzel and McDonald lacked training and experience in oncology or drug evaluation. *Id.* at 150a-151a. The court also relied on two affidavits, apparently executed for another proceeding, in which Drs. Gurchot and Leake stated that Laetrile was used experimentally between 1934 and 1945 and was recognized then as being safe. *Id.* at 31a-32a n. 23. These assertions are in dispute (*id.* at 206a-208a) and, in any event, are not supported by data purporting to show Laetrile's nontoxicity. The composition, purity, and strength of the Laetrile Gurchot and Leake discuss are different from those of the Laetrile in use today. *Id.* at 171a-172a.



terms, must fall because of the erroneous factual assumption on which it is based.

**B. The Constitutional Right of Privacy Does Not Include a Right to Use Unproven or Ineffective Drugs**

This case arises against the background of a long Anglo-American tradition of government protection of the public from unsafe, worthless, or fraudulent foods and drugs. As the historical survey in the Appendix to this brief notes, the sale of food "not wholesome for man's body" was first prohibited by an English statute passed in 1266 (51 Henry III, c. 6), and the regulation of drugs in England dates from the mid-sixteenth century.<sup>41</sup> The advances of modern science since the mid-nineteenth century have made possible, for the first time in human history, the broad application of scientific principles to the treatment of human disease. These advances have also made possible more precise evaluations of the identity and effects of drugs. They have thereby established the basis for a system of drug regulation in this country that protects the public in a rational and scientifically informed way against unsafe or ineffective drugs.

The constitutional privacy claim asserted by respondents and upheld by the district court in this case thus challenges the foundations of a centuries-old function of government. The challenge takes aim, not at the administrative action of the Commissioner, but at the Federal Food, Drug, and Cosmetic Act

<sup>41</sup> See G. Clark, *A History of the Royal College of Physicians of London* 80, 82-83 (1964); see App., *infra*, 1a-3a.

itself, since the Commissioner has correctly applied the Act in reaching his decision (see Points I and II, *supra*). If the challenge were to succeed, it would disable not only the federal government, but the states as well, from protecting the public against worthless drugs. The challenge, however, must fail, for it has no support in the privacy decisions of this Court.

1. As the Court has observed, "Virtually every governmental action interferes with personal privacy to some degree. The question in each case is whether that interference violates a command of the United States Constitution." *Katz v. United States*, 389 U.S. 347, 350 n.5 (1967). We do not dispute that the personal health care of cancer patients who wish to take Laetrile—as well as the financial interests of those who manufacture and distribute the drug—is affected by the application to Laetrile of the safety and effectiveness requirements of the Act and the consequent prohibition of the drug's importation or introduction into interstate commerce until the statutory requirements are met.<sup>42</sup> But the Constitution does not necessarily forbid that result. This Court's decisions recognizing a constitutional right of privacy do not deny Congress the power to protect the public health and welfare by enacting laws to assure that medical drugs available to the public are safe and effective for their intended use, even if such laws

<sup>42</sup> See Sections 301(d) and 304 of the Act, 21 U.S.C. 331(d) and 334; see also 18 U.S.C. 545. No provision of federal law directly prohibits personal use or affects any supply that has neither been imported nor had any connection with interstate commerce.

interfere with an individual's access to an unproven drug that a court believes to be nontoxic. To read the Court's decisions as requiring such a result would be to invoke the right of privacy in place of freedom of contract, see *Lochner v. New York*, 198 U.S. 45 (1905), as a basis for substituting the will of the courts for the judgment of Congress concerning how best to protect the public health and welfare. See *Whalen v. Roe*, 429 U.S. 589, 596-597 (1977).

This Court's recognition of a constitutional right of privacy has its main roots in the dissenting opinion of Mr. Justice Brandeis in *Olmstead v. United States*, 277 U.S. 438, 471-485 (1928), and the decision of the Court in *Griswold v. Connecticut*, 381 U.S. 479 (1965). In *Olmstead*, Mr. Justice Brandeis discerned in the Constitution an intent to "protect Americans in their beliefs, their thoughts, their emotions and their sensations" and in "the right to be let alone—the most comprehensive of rights and the right most valued by civilized men." 277 U.S. at 478. In *Griswold*, this Court identified a "zone of privacy created by several fundamental constitutional guarantees" (381 U.S. at 485), and held that a state law making it a crime for any person to use any drug or article to prevent conception violated a right of marital privacy that falls within that zone.

The dimensions of the constitutional right of privacy have gradually emerged since *Griswold*. In *Whalen v. Roe*, 429 U.S. 589, 599 (1977), the Court described its "privacy" cases as involving "at least two different kinds of interests." One it defined as

"the individual interest in avoiding disclosure of personal matters," and the other as "the interest in independence in making certain kinds of important decisions." *Id.* at 599-600. To these may be added an interest in freedom from unwarranted intrusions into the human body. See *Schmerber v. California*, 384 U.S. 757, 766-767 (1966).

Nothing suggests that the nondisclosure interest is involved in this case. Neither can it be said that intrusions into the human body are involved, for the federal laws at issue here do not require cancer patients to undergo particular forms of treatment, or any treatment at all.<sup>43</sup>

In holding that the Constitution guarantees a right to use substances not proven toxic "in connection with one's own personal health-care" (Pet. App. 41a), the district court relied primarily on cases involving

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<sup>43</sup> The Court has upheld physical intrusions in *Jacobson v. Massachusetts*, 197 U.S. 11 (1905) (compulsory smallpox vaccination); *Buck v. Bell*, 274 U.S. 200 (1927) (compulsory sterilization of certain persons adjudged mentally defective); and *Schmerber v. California*, *supra*, 384 U.S. 757 (compulsory drawing of blood sample for analysis of alcohol content). And the Court has relied on *Jacobson* and *Buck* to reject the suggestion that "an unlimited right to do with one's body as one pleases bears a close relationship to the right of privacy previously articulated in the Court's decisions." *Roe v. Wade*, 410 U.S. 113, 154 (1973). Those cases can also be viewed, however, as involving intrusions into a constitutionally protected zone of privacy that were warranted by what were judged to be compelling state interests, expressed through laws reasonably related to those interests. See page 68, *infra*.

the privacy interest in "independence in making certain kinds of important decisions"—particularly the cases of *Doe v. Bolton*, 410 U.S. 179 (1973), and *Roe v. Wade*, 410 U.S. 113 (1973), both concerned with abortion.<sup>44</sup> But this Court's view of that line of cases makes it clear that they do not support the claim made here. The Court has characterized those cases as dealing with "matters relating to marriage, procreation, contraception, family relationships, and child rearing and education." *Paul v. Davis*, 424 U.S. 693, 713 (1976); see *Whalen v. Roe*, *supra*, 429 U.S. at 600 n.26 (quoting same statement). The right claimed here of caring for one's health by obtaining a particular drug without government hindrance does not fall into any of those categories. Without belittling the desperate predicament of a person threatened with death from cancer or other disease, and without denying that life may be at stake in any medical decision made by or for that person, the fact remains that the decision to take a particular drug in an effort to prolong life or cure disease is a technical, instrumental decision—a decision as to how best to achieve a hoped-for medical effect. It is not among the "certain kinds of important decisions" to which the Court

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<sup>44</sup> Other cases in this category include *Loving v. Virginia*, 388 U.S. 1 (1967) (choice of spouse); *Griswold v. Connecticut*, *supra* (decision to use contraceptives); *Pierce v. Society of Sisters*, 268 U.S. 510 (1925) (choice of children's school); *Meyer v. Nebraska*, 262 U.S. 390 (1923) (choice of a legitimate vocation).

referred in *Whalen v. Roe*, *supra* (429 U.S. at 599-600).<sup>45</sup>

2. This Court has recognized that decisions of the kind at issue here, involving the efficacy or safety of drugs or medical treatments, are not among the kinds of decisions protected by the constitutional right of privacy.<sup>46</sup> In a series of abortion and contraception

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<sup>45</sup> Nor does the claimed constitutional right of free choice with respect to medical drugs implicate the First Amendment values that have informed decisions such as *Stanley v. Georgia*, 394 U.S. 557, 565 (1969) (holding that a state may not prohibit possession of obscene materials in one's home). Cf., e.g., *United States v. 12 200-Ft. Reels of Film*, 413 U.S. 123, 128 (1973) (importation of obscene matter may be prohibited even when for private use only; "[t]o allow such a claim would be not unlike compelling the Government to permit importation of prohibited or controlled drugs for private consumption as long as such drugs are not for public distribution or sale").

<sup>46</sup> The authority of government, in some circumstances, to override individual choice in matters not affecting others was reaffirmed in *Paris Adult Theater I v. Slaton*, 413 U.S. 49 (1973). The Court stated: "[F]or us to say that our Constitution incorporates the proposition that conduct involving consenting adults only is always beyond state regulation is a step we are unable to take" (*id.* at 68), and explained (*id.* at 68 n.15):

The state statute books are replete with constitutionally unchallenged laws against prostitution, suicide, voluntary self-mutilation, brutalizing "bare fist" prize fights, and duels, although these crimes may only directly involve "consenting adults". Statutes making bigamy a crime surely cut into an individual's freedom to associate, but few today seriously claim such statutes violate the First Amendment or any other constitutional provision. [Citations omitted.]



cases the Court has emphasized that, although the laws in question were unconstitutional because they impinged on the right of independent decision-making with respect to pregnancy and procreation, government restrictions on that right are justified when they serve compelling interests in "safeguarding health, [or] in maintaining medical standards \* \* \*." *Roe v. Wade*, *supra*, 410 U.S. at 154; see also *id.* at 162-164; *Doe v. Bolton*, *supra*, 410 U.S. at 189; *Planned Parenthood of Missouri v. Danforth*, 428 U.S. 52 (1976); *Carey v. Population Services International*, 431 U.S. 678, 685-686 (1977). Indeed, in *Roe v. Wade* the Court observed that "[t]he State has a legitimate interest in seeing to it that abortion, like any other medical procedure, is performed under circumstances that insure *maximum* safety for the patient" (410 U.S. at 150; emphasis added), and the Court listed a number of the measures that a state may permissibly take to regulate abortion in furtherance of its interests "in the areas of health and medical standards" (*id.* at 149).<sup>47</sup> Thus, the abortion

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<sup>47</sup> The government may require that abortions be performed (after the first trimester) only at licensed institutions that "insure maximum safety for the patient" and may prohibit any abortion performed by a person not a physician (*id.* at 150, 165). The state may also totally prohibit an abortion during the third trimester of pregnancy (*id.* at 165); its interest in doing so is constitutionally justified even apart from its interest in protecting prenatal life, since "the State retains a definite interest in protecting the woman's own health and safety when an abortion is proposed at a late stage of pregnancy" (*id.* at 150). Of course, the state may impose these restrictions on a woman's abortion right even when the woman is fully aware of the risks and willing to take them.

laws at issue in *Roe v. Wade*, *Doe v. Bolton*, and *Planned Parenthood v. Danforth* were struck down not because they interfered in health care decisions, but because they demonstrably were not designed to serve any health interest.

This point was made most clearly in *Planned Parenthood v. Danforth*, where the Court struck down a state prohibition of a particular abortion procedure, saline amniocentesis. Quoting *Roe v. Wade*, the Court defined the issue before it as "[w]hether the flat prohibition of saline amniocentesis is a restriction which 'reasonably relates to the preservation and protection of maternal health.'" 428 U.S. at 76. The Court cited voluminous record evidence of the safety and effectiveness of saline amniocentesis, in comparison with other available abortion procedures, and concluded that the state prohibition bore no reasonable relationship to protection of maternal health. 428 U.S. at 78-79.

The Court's recognition of the government's interest in protecting the health of its citizens was reiterated in *Carey v. Population Services International*, *supra*, 431 U.S. at 678. There, while disclaiming any view that "there is an independent fundamental 'right of access to contraceptives'" (*id.* at 688), the Court struck down a law restricting access to that particular category of drugs and medical devices<sup>48</sup>

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<sup>48</sup> "Barrier" contraceptives are medical devices regulated under the Medical Device Amendments of 1976, Pub. L. No. 94-295, 90 Stat. 579 (1976). Birth control pills are drugs regulated under the drug provisions of the Food, Drug, and Cosmetic Act.

"because such access is essential to exercise of the constitutionally protected right of decision in matters of child-bearing" (*ibid.*) (citing *Roe v. Wade*, *supra*, and *Griswold v. Connecticut*, *supra*). Still, the Court did not hold that there is a constitutional right of access to all contraceptives, regardless of their safety and efficacy. The Court cited the Federal Food, Drug, and Cosmetic Act—including the drug regulation provisions at issue in this case—as among federal and state laws "that comprehensively regulate hazardous drugs and devices" (431 U.S. at 690 n.9), and suggested that in light of those laws the state anti-contraceptive statute at issue in *Carey* did not serve any "health-related interest" (*ibid.*).<sup>49</sup> The Court also pointed out that the statute was not "designed to serve as a quality control device" (*id.* at 691).

Thus, *Carey*, *Planned Parenthood*, and the other cases invalidating laws restricting the individual's decision with respect to pregnancy and procreation have all distinguished, and preserved, the government's interest in regulation designed to protect the public's health.<sup>50</sup> In this case, we deal with the statute that

<sup>49</sup> In *Eisenstadt v. Baird*, 405 U.S. 438 (1972), where the Court struck down under the Equal Protection Clause a state statute prohibiting the distribution of contraceptives to unmarried persons, it similarly referred to "the federal and state laws *already* regulating the distribution of harmful drugs," including the Federal Food, Drug, and Cosmetic Act (*id.* at 452; emphasis in original), as part of its analysis of why the state law at issue did not serve a health purpose.

<sup>50</sup> For a vindication of that interest, see *Fitzgerald v. Porter Memorial Hospital*, 523 F.2d 716, 721 (7th Cir. 1975) (Stevens, J.), cert. denied, 425 U.S. 916 (1976), holding that

provides the public's primary protection against unsafe, ineffective, or fraudulent drugs. This statute is specifically designed to serve "as a quality control device." Its clear and direct relationship to health protection is undeniable. At the same time, this case involves no claim bound up with the constitutionally protected right of independent decision-making concerning marriage, pregnancy, and procreation. The Court's privacy decisions hence do not support, but reject, the claim made here of a constitutional right to use a particular medical drug.<sup>51</sup>

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"the so-called right of marital privacy does not include the right of either spouse to have the husband present in the delivery room of a public hospital which, for medical reasons, has adopted a rule requiring his exclusion."

<sup>51</sup> In his concurring opinion in *Doe v. Bolton*, Mr. Justice Douglas characterized "the freedom to care for one's health and person" as "fundamental" and, therefore, "subject to regulation [only] on a showing of 'compelling state interest.'" 410 U.S. at 213. The district court discerned in this language a right of privacy protecting the acquisition and use of Laetrile (Pet. App. 36a). Mr. Justice Douglas did not go so far, for he recognized the "legitimate objective of preserving the mother's health [that] clearly supports [some abortion] laws." 410 U.S. at 216. Because the Georgia statute "outlaw[ed] virtually all such operations," he concluded that it could not be "seriously urged that so comprehensive a ban is aimed at protecting the woman's health." 410 U.S. at 216-217. The Federal Food, Drug, and Cosmetic Act, by contrast, does not comprehensively ban all drugs for cancer treatment, but only those not shown to be safe and effective. In any event, Mr. Justice Douglas's conception of health care as a separate privacy right under the Constitution has not won the support of the Court.

3. This conclusion is confirmed by a statement the Court made in *Whalen v. Roe*, 429 U.S. 589 (1977). The question there was whether a state may record in a centralized computer file the names and addresses of persons who obtain certain prescription drugs for which there is a lawful and an unlawful market; the Court held that it may, without violating any constitutional right to privacy. In discussing the privacy claim, the Court commented: "the State no doubt could prohibit entirely the use of particular Schedule II drugs \* \* \*" (*id.* at 603).<sup>52</sup> Schedule II drugs "have accepted uses in the amelioration of pain and in the treatment of [various diseases]" (*id.* at 593 n.8); they are safe and effective, but are also liable to abuse. If a state may prohibit entirely the use of such drugs—which can provide important therapeutic benefits to some patients—then *a fortiori* the government in this case may prohibit interstate commerce in a drug that has no recognized medical use in the treatment of the life-threatening disease for which it is recommended, and which has a potential for harming, at the least, those patients who are deterred by the drug's availability from seeking effective treatment.

<sup>52</sup> In a footnote at this point (*id.* at 603 n.30) the Court stated: "It is, of course, well settled that the State has broad police powers in regulating the administration of drugs by the health professions," citing *Robinson v. California*, 370 U.S. 660, 664-665 (1962); *Minnesota ex rel. Whipple v. Martinson*, 256 U.S. 41, 45 (1921); and *Barasky v. Board of Regents*, 347 U.S. 442, 449 (1954).

The dictum in *Whalen v. Roe* thus underscores the lesson of the Court's privacy decisions. As the abortion and contraception cases expressly recognize, the government has an interest in the health of its citizens which justifies health-related restrictions on established constitutional privacy rights. If that is so, then surely freedom from government health regulation of drugs is not itself a constitutionally protected right.

4. The contours of this case are deceptively narrow. The constitutional claim may be urged in this Court only in support of a judgment that prohibits the government from interfering with access by "terminally ill" cancer patients to supplies of Laetrile intended for intravenous administration under the direction of a physician.<sup>53</sup> But the logic of the claim goes much further. If, as the district court held, there is a constitutional right of access to any drug not *proven* toxic, then it is difficult to see how the safety and efficacy requirements of the Act can be constitutionally enforced with respect to *any* drug if a court decides the drug is nontoxic, a physician somewhere is willing to prescribe it, and an individual wishes to take it. Already, a group of patients suffering from adrenal corticoid insufficiency, a condition treatable by the use of steroid compounds approved under Section 505 of the Act, have brought suit in the same district court that decided this case to prohibit the FDA from enforcing the requirements of the Act with respect to a new drug described as

<sup>53</sup> See page 2, note 1, *supra*.



adrenal corticol extract.<sup>54</sup> Other patients claiming a constitutional right to receive marijuana for medical purposes have filed district court suits to vindicate that right.<sup>55</sup> And the constitutional claim would be equally fatal, of course, to state as to federal regulation. We submit that this Court's privacy decisions require no such results.

**C. Application to Laetrile of the Safety and Efficacy Requirements of the Food, Drug, and Cosmetic Act Is a Reasonable Means of Serving a Compelling Government Interest in Protecting the Public Health**

Even "fundamental" rights are not absolute; they may constitutionally be restricted if the restrictions are justified by a "compelling" governmental interest. *Roe v. Wade*, *supra*, 410 U.S. at 155; *Carey v. Population Services International*, *supra*, 431 U.S. at 686. If this Court were to recognize, contrary to our submission, a constitutional right of access to unproven drugs "in connection with one's own personal health-care," enjoyed either by terminally ill patients or by members of the public generally, it should nonetheless reject the constitutional claim in this case. It should do so on the ground that application of the Food, Drug, and Cosmetic Act to Laetrile is justified by compelling governmental interests in pro-

<sup>54</sup> *American Academy of Medical Preventives v. Califano*, No. 79-60-E (W.D. Okla., filed Jan. 16, 1979).

<sup>55</sup> See, e.g., *Mayerson v. Bensinger, et al.*, No. 78-2707 (E.D. Pa., filed Aug. 11, 1978); *Hartz v. Bensinger, et al.*, 461 F. Supp. 431 (E.D. Pa. 1978).

tecting the public health, reinforced by a legitimate interest in preventing fraud.

1. There is a compelling governmental interest in maintaining a system for the scientific evaluation of the safety and effectiveness of drugs before they are permitted to be marketed. Laymen generally are not qualified to determine whether a particular course of therapy will be effective. Even individual physicians are not in a position to determine scientifically which drugs on the market are effective. *Upjohn Co. v. Finch*, 422 F.2d 944, 952-954 (6th Cir. 1970). As a consequence, Congress decided that an expert scientific agency should make that determination—on the basis of information submitted by the manufacturer or promoter—before the drug is permitted to be marketed.

When Congress amended the Food, Drug, and Cosmetic Act in 1962, the House Report noted:

[M]any new drugs that have cleared the safety requirements of the law are marketed with unproved claims of therapeutic effectiveness. As a result, good medical practice is hampered, and the consumer is misled until, perhaps years later, the Government has gathered the necessary evidence to sustain its burden of proving the violation in court.

H.R. Rep. No. 2464, 87th Cong., 2d Sess. 3 (1962). The effect of invalidating the statute or judicially exempting Laetrile would be to deprive the public of assurance that drugs on the market have "the reliability and effectiveness" Congress intended. S.

Rep. No. 1744 (Part 1), 87th Cong., 2d Sess. 17 (1962).<sup>56</sup>

Having reasonably concluded that unsafe or ineffective drugs are harmful to the public health, Congress established a system requiring the Commissioner to determine that a new drug is safe and effective before it may be marketed in interstate commerce. In this case, acting within the authority granted him by the statute, the Commissioner has determined that Laetrile has not met the requirements imposed by the Act. That the factual issues may be in dispute does not disable the government from acting, for this Court long ago established that a legislature is "not compelled to commit a matter involving the public

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<sup>56</sup> The history of cancer therapy in this country confirms the justification for legislative concern that, without pre-marketing clearance, useless drugs would flourish to the detriment of the public health. As the Commissioner found, there has been a long and sorry history of cancer quackery, during which "literally thousands of supposed remedies for cancer" have been promoted. Pet. App. 212a-217a. For example, in the 1940's and early 1950's cancer patients paid as much as \$300 per injection for the worthless Koch's Synthetic Antitoxins. *Id.* at 214a. Harry Hoxsey promoted his unproven cancer remedy for more than 30 years in spite of numerous local, state, and federal court actions, until a permanent injunction was finally issued in 1960, at which time more than 10,000 patients were receiving the remedy. *Id.* at 214a-215a. Krebiozen was another remedy popular in the 1960's. *Id.* at 215a-217a. (The proponents of Krebiozen also brought a suit to force the FDA to allow the marketing of an unapproved new drug. See *Rutherford v. American Medical Association*, 379 F.2d 641 (7th Cir. 1967), cert. denied, 389 U.S. 1043 (1968).)

health to the final decision of a court or jury." *Jacobson v. Massachusetts*, *supra*, 197 U.S. at 30.<sup>57</sup> Congress has sought to preserve public and professional confidence in the safety and efficacy of the drug supply by committing such decisions to the Commissioner. This interest is a compelling one, and the resulting restriction on the interstate distribution of Laetrile is reasonably and indispensably related to it.

2. The government also has a compelling interest in preventing the marketing of ineffective drugs in order to promote the timely treatment of illness with safe and effective drugs. As Senator Kefauver pointed out when introducing the 1962 amendments: "An otherwise completely safe drug can be dangerous to the patient if it does not have the therapeutic effect in use which it is represented to have." 107 Cong. Rec. 5640 (1961).<sup>58</sup> This fact is poignant because a

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<sup>57</sup> See also *Fitzgerald v. Porter Memorial Hospital*, *supra*, 523 F.2d at 721:

[T]he dispute within the medical profession as to the propriety and safety of permitting the husband to be present during the routine birth is not one that should be resolved by substituting our judgment for the professional judgment of the staff of defendant hospital. [Footnote omitted.]

<sup>58</sup> The legislative concern that credulous and desperate laymen will rely on the claims made for ineffective drugs and thus delay treatment by recognized therapy, or that even physicians will believe false claims and prescribe ineffective drugs in place of more reliable substitutes, is well justified. See, e.g., *Durovic v. Richardson*, *supra*, 479 F.2d at 251; *Upjohn Co. v. Finch*, 422 F.2d 944, 953 (6th Cir. 1970);

significant number of cancer patients can be cured, or enabled to live longer, by legitimate therapy. Pet. App. 227a, 268a; see page 73, note 61, *infra*. The availability of Laetrile encourages delay in obtaining legitimate therapy, or avoidance of such therapy altogether. Pet. App. 228a-242a. And even after patients begin treatment with effective therapy, the readily acknowledged side effects and hazards of that therapy may cause them to abandon it when it might still be beneficial, and turn instead to Laetrile. *Ibid*. The drug's promoters, playing on the patients' fears, actively encourage this process (*id.* at 230a-233a).<sup>60</sup>

The district court was concerned about the "terminally ill" cancer patient. But the record reflects that the prospective identification of a patient as "terminal" is frequently inaccurate, since "[m]any patients who are critically ill respond to modern day management of cancer." Pet. App. 268a. Moreover, there is no proof that Laetrile will not "interfere with

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*United States v. Nutrition Service, Inc.*, 227 F. Supp. 375, 388 (W.D. Pa. 1964), *aff'd per curiam*, 347 F.2d 233 (3d Cir. 1965).

<sup>60</sup> The district court suggested that constitutional protection may attach to the use of Laetrile because it has a "placebo" effect. Pet. App. 24a, 38a. The placebo effect can occur when an authority figure (usually a physician) administers a drug to the patient with a statement that the drug will prevent cancer, relieve his pain or help him get well. But the placebo effect operates precisely and solely because the patient is deceived into believing that he is receiving a therapeutically effective drug.

the metabolism of and compromise the effects from known anticancer treatments" (*id.* at 271a).<sup>60</sup>

In addition, government acquiescence in the use of Laetrile in the injectable form by the terminally ill may suggest to other cancer patients, including ones in the early stages of the disease and quite susceptible to conventional treatment, that the government accepts the drug as being of some value. They may consequently attempt to secure it, quite possibly in the potentially toxic tablet form, either at Mexican clinics or through illicit channels, to the neglect of their conventional therapy and the detriment of their health. See Pet. App. 268a-271a.<sup>61</sup>

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<sup>60</sup> "Some have suggested that, if legalized, Laetrile should be used only on hopelessly ill patients with cancer. These patients, however, present special problems which have not been adequately investigated. For instance, the acute toxicity of Laetrile in tumor-bearing animals is much greater than is the acute toxicity of Laetrile in non-tumor-bearing animals. This suggests that the more tumor that is present, the more toxic the Laetrile becomes \* \* \*. In addition, these patients invariably have liver and renal damage \* \* \*. Laetrile is detoxified by rhodenase which is found in high levels in the liver. Is this same high level found in a cancerous liver? We have no data on this. \* \* \* What is the effect of kidney failure on Laetrile's toxicity? Again, the data are not available." Lewis, *Laetrile*, 127 West. J. Med. 55, 59-60 (1977).

<sup>61</sup> "[R]ecent Trends in Survival of Cancer Patients, [1960-1971] shows that substantial progress has been made in all 17 tumor types indexed. The percent increase in five-year survival rates ranges from 0 for one disease only \* \* \* to 700 percent for acute lymphocytic leukemia in females. The average increase in five year survival for all patients was 75 percent." Lewis, *supra*, 127 West. J. Med. 55. The present survival rate is likely to be higher, but is not known since "the major ad-



Despite the limitation of the court of appeals' judgment to injectable Laetrile provided for the terminally ill, some leakage of drug shipments to persons not within that class may be expected. Indeed, there is evidence that this has occurred in the distribution of Laetrile under the system established by the district court. The affidavit of Gerald M. Rachanow, Consumer Safety Officer in the FDA's Bureau of Drugs (A. 81-84), states that in some instances supplies of Laetrile ordered by patients in the certified class, through physicians designated as purchasing agents, have not been delivered to those patients (A. 82, 83). In other instances, orders have been placed for supplies of Laetrile which the designated patients do not wish to receive (*ibid.*). These practices create supplies of Laetrile available for sale to patients not in the certified class (A. 83-84).<sup>62</sup>

vances in the past decade in chemotherapy are yet to be adequately recorded by this survey." *Id.* at 56. In view of present progress, abstinence from effective therapy in favor of Laetrile is all the more damaging to the public health.

<sup>62</sup> The course of cancer in the human body is irregular and unpredictable. It is often marked by spontaneous remissions, which may last for extended periods of time (Pet. App. 240a-241a). When a spontaneous remission occurs while a patient is taking a particular drug, it is easy to say that the drug caused the remission; one of the great difficulties in cancer research is distinguishing between spontaneous remissions and those due to a particular drug the patient is taking. If the use of Laetrile or other unproven drugs by cancer patients were permitted, spontaneous remissions occurring during such treatment would induce additional cancer patients to forsake approved (but more painful and inconvenient) treatments in the vain hope that the unproved, and in fact ineffective, drug will provide a cure.

3. Even apart from public health considerations, the government has a strong interest in preventing promoters of useless drugs from deceiving the public.<sup>63</sup> An ineffective drug is a fraud, which wastes the financial resources of the patient and his family. Accordingly, this Court has stated that Congress "surely has great leeway in setting standards for releasing on the public, drugs which may well be miracles or, on the other hand, merely easy money-making schemes through use of fraudulent articles labeled in mysterious scientific dress." *Weinberger v. Hynson, Westcott & Dunning, Inc., supra*, 412 U.S. at 622. The social and economic costs that ineffective cancer treatments impose on society are costs Congress sought to prevent when it enacted the statute at issue here.

4. Finally, constitutional protection for Laetrile would inevitably mean constitutional protection for other unproven drugs, both for cancer and for other diseases. Cancer, of course, is not the only disease that may be fatal, and cancer patients not the only ones who may be "terminally ill." Upholding of the district court's constitutional ruling could be expected to produce a heyday for unproven cures, beneficial only to those who sell them. The government's interest in preventing this result, and preserving the public protection now afforded by the Act, is compelling.

<sup>63</sup> Although commercial speech enjoys First Amendment protection, the state may impose limitations designed to prohibit misleading or deceptive commercial advertising. See *Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976).

## CONCLUSION

The judgment of the court of appeals should be reversed.

Respectfully submitted.

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## APPENDIX

GOVERNMENT REGULATION OF DRUGS:  
AN HISTORICAL SUMMARY

Laws protecting the public from unsafe and fraudulent foods and drugs have a long history in Anglo-American jurisprudence. The sale of food "not wholesome for man's body" was prohibited by an English statute passed in 1266.<sup>1</sup> A 1511 statute provided for punishment of persons who "by crafty means" adulterated edible oils "to the great loss, jeopardy, danger and deceit of [the King's] subjects \* \* \*."<sup>2</sup> The sale of unwholesome food was a misdemeanor at common law.<sup>3</sup>

This English tradition was carried over to the colonies, which enacted laws regulating foods as early as 1646.<sup>4</sup> Regulation of foods on the state level continued until enactment of the federal Pure Food and Drugs Act of 1906. Pub. L. No. 59-384, 34 Stat. 768 (1906).<sup>5</sup>

<sup>1</sup> 51 Henry III, c. 6 (1266), 1 Pickering, *Statutes at Large* 49-50 (1762) (hereinafter cited as Pickering). See generally Hutt, *The Basis and Purpose of Government Regulation of Adulteration and Misbranding of Food*, 33 FDC L.J. 505 (1978); Hart, *A History of the Adulteration of Food Before 1906*, 7 FDC L.J. 5 (1952).

<sup>2</sup> 3 Henry VIII, c. 14 (1511), 4 Pickering 118-119.

<sup>3</sup> Hutt, *Criminal Prosecution for Adulteration and Misbranding of Food at Common Law*, 15 FDC L.J. 382, 383-390 (1960).

<sup>4</sup> See Hutt, *supra* note 1, at 507-508, n.19.

<sup>5</sup> See Hutt, *supra* note 1, at 509.

Efforts to protect the public health through regulation of medicines and of those who sold and administered them roughly paralleled our forebearers' increasing regulation of the safety and suitability of the food supply. However, for practical and superstitious reasons, public protection against unfit remedies was more difficult to achieve than protection against unwholesome foods.

Until the mid-nineteenth century the history of medicine was in large part the history of ineffective, and quite often toxic, remedies. Before the advent of modern chemistry in the 1850's, the composition of drugs could be concealed with little difficulty.<sup>6</sup> Scientific assessment of safety came later, and of effectiveness, later still. The impetus and methodology for scientific evaluation of drug effectiveness were not developed until the early part of this century and did not achieve acceptance until around the time of the second world war.<sup>7</sup>

Healing has always had mystical and religious overtones. Before the development of modern science,

<sup>6</sup> J. Young, *The Toadstool Millionaires* 209-210 (1961) [hereinafter cited as Young].

<sup>7</sup> See Irons, *The Clinical Evaluation of Drugs*, 93 JAMA 1523-1524 (1929); Leake, *The Pharmacologic Evaluation of New Drugs*, 93 JAMA 1632-1634 (1929); Atkins, *Conduct of a Controlled Clinical Trial*, Brit. Med. J. No. 5510 at 377-379 (1966); Van Winkle, et al., *Laboratory and Clinical Appraisal of New Drugs*, 126 JAMA 958-961 (1944); H. Gold, "Experience in Human Pharmacology," in *Quantitative Methods in Human Pharmacology and Therapeutics* (1959); Gaddum, *Clinical Pharmacology*, 47 Proc. Royal Soc. Med. 195-204 (1954); B. Barber, *Drugs and Society* 19 (1967).

man "naturally ascribe[d] his diseases either to the wrath of a good being or the malice of an evil being."<sup>8</sup> Thus, until roughly the sixteenth century, magicians, priests and kings were regarded as specially qualified for the healing of the sick.<sup>9</sup> The first tentative official efforts at regulation of those practicing medicine date from the passage of the Licensure Act of 1511, which prohibited unlicensed physicians from practicing medicine.<sup>10</sup> In 1518 the College of Physicians, by a Royal Charter from Henry VIII, was given authority to examine physicians' prescriptions for internal and external medicines and to punish "delinquencies" in the medicinal uses "by fines, amercement, imprisonment or other \* \* \* fitting ways."<sup>11</sup> Parliament ratified the Royal Charter in 1523, and, by an Act of Common Council in 1525, required pharmacists to accept prescriptions only from duly qualified and registered practitioners and to keep those prescriptions on file so that members of the College could determine whether the compounds were suitable for medicinal use.<sup>12</sup> By Act of Parliament in 1540, members of the College called "censors" were

<sup>8</sup> E. Maple, *Magic, Medicine and Quackery* 14 (1968) [hereinafter cited as Maple].

<sup>9</sup> Maple, *supra* note 8, at 13-62.

<sup>10</sup> 3 Henry VIII, c. 2, G. Clark, *A History of the Royal College of Physicians of London*, Volume I, 54-55 (1964) [hereinafter cited as Clark].

<sup>11</sup> Clark, *supra* note 10, at 58, 60. Henry VIII was a dedicated apothecary himself and is reported to have devised 230 medical prescriptions. Maple, *supra* note 8, at 75.

<sup>12</sup> Clark, *supra* note 10, at 79.



given additional authority to enter apothecary shops and to condemn unfit medicines.<sup>13</sup>

This effort at comprehensive drug regulation was short-lived. In reaction to the refusal of physicians to treat the poor, Parliament passed in 1542 another statute commonly referred to as the "Quacks' Charter." The Charter castigated the medical profession as "minding only their own lucre" and as having "troubled and vexed \* \* \* honest men and women whom God hath endowed with the knowledge of the nature, kind and operation of certain herbs, rootes and waters." The Charter granted to folk-healers the authority to cure all maladies apparent on the surface of the body by means of plasters, poultices, and ointments.<sup>14</sup> Quackery thus became the officially sanctioned medicine for the poor. However, in 1553 the authority of the College of Physicians to enter apothecary shops and inspect drug prescriptions and medicines was reinstituted by Parliament, in an Act which additionally made refusal to permit inspection subject to a fine of ten pounds.<sup>15</sup>

Enforcement efforts still were not undertaken on a comprehensive scale; they consisted mainly of fines and condemnation proceedings against patently defective medical merchandise<sup>16</sup> and of imprisonment

<sup>13</sup> *Id.* at 82-83, 92.

<sup>14</sup> *Id.* at 86. See also Maple, *supra* note 8, at 65.

<sup>15</sup> Clark, *supra* note 10, at 88.

<sup>16</sup> Maple, *supra* note 8, at 95 (condemnation in 1671 of an entire stock of defective spectacles).

of "imposters."<sup>17</sup> In 1748, the Apothecaries' Act was passed to protect the public against unqualified pill-makers.<sup>18</sup> Nevertheless, England remained the province of those peddling unproven remedies such as "Payne's Medicine for the cure of forgetfulness."<sup>19</sup>

The situation was similar in the American colonies. "[T]he emigrant who sought refuge in the New World would find that the medical quack had arrived before him \* \* \*."<sup>20</sup>

American attempts to curtail fraudulent cures date at least to 1630, when a Massachusetts colonist was fined (or whipped) for vending a cure for scurvy determined to be "a water of no worth nor value."<sup>21</sup> In 1649, Massachusetts passed "An Act Respecting Chirurgions, Midwives and Physicians," prohibiting them from "any act contrary to the known approved Rules of Art \* \* \*"; New York passed a similar act in 1684.<sup>22</sup> In 1699 Massachusetts passed a quar-

<sup>17</sup> Wright and Dobbs, *Quacks Through The Ages*, 105 J. Roy. Soc. Arts. 161, 162-163 (1957).

<sup>18</sup> Maple, *supra* note 8, at 113.

<sup>19</sup> Maple, *supra* note 8, at 126. Following the earthquake of 1755 in Lisbon, one English vendor is reported to have offered pills "good for the earthquake." *Id.*

<sup>20</sup> Maple, *supra* note 8, at 157.

<sup>21</sup> Young, *supra* note 6, at 16-17.

<sup>22</sup> General Laws and Liberties of the Massachusetts Colony, page 28 (1672); 1 Colonial Laws of New York, ch. 5, page 146 (1894). These Acts may be found in the American-British Law Division, Library of Congress, by courtesy of James W. Elder, Librarian.

antine regulation to control smallpox epidemics.<sup>23</sup> Virginia passed an act in 1736 to regulate "the true value of the medicines administered by any practitioner in phisic," which required that the composition of "any pills, bolus, portion \* \* \* or any medicines" be expressed in "every particular" upon the practitioner's bill.<sup>24</sup> In 1773 the Connecticut colonial assembly outlawed the activities of mountebanks for a variety of social ills and the sale of "unwholesome and oftentimes dangerous drugs."<sup>25</sup> Continental Army commanders ordered the inoculation of troops in Boston shortly before the Declaration of Independence, in 1776, and General Washington ordered mass inoculation on January 6, 1777.<sup>26</sup>

Legislation to control the quality of drugs began in earnest with an 1808 Louisiana statute proscribing drug adulteration; by 1865 at least 14 states had passed legislation to control the quality of drugs.<sup>27</sup> The Code of Tennessee referred to adulteration that would "lessen the efficacy or change the operation [of

<sup>23</sup> J. Blake, *Public Health in the Town of Boston, 1630-1822* 32-36 (1959).

<sup>24</sup> 4 Henings, *Statutes at Large* 509-510 (1814).

<sup>25</sup> Young, *supra* note 6, at 191.

<sup>26</sup> S. Bayne-Jones, *The Evolution of Preventive Medicine in the United States Army, 1607-1939* 51-52 (1968). See also F. Packard, *History of Medicine in the United States*, 83-84, 578 (1963).

<sup>27</sup> J. Blake, *Safeguarding the Public, Historical Aspects of Medical Drug Control* 100-101 (1970) [hereinafter cited as Blake].

drugs in a manner] injurious to health."<sup>28</sup> The first federal law was the Import Drugs Act of 1848, ch. 70, 9 Stat. 237.<sup>29</sup> It was reported that in the first ten months following enactment of this statute, 90,000 pounds of drugs were refused admission to the country after examination of their quality, purity, and fitness for medical purposes.<sup>30</sup>

By 1879, at least 25 states and territories had enacted statutes to control drug adulteration.<sup>31</sup> A steady growth in state regulation of adulterated drugs continued, and by 1900, 45 states and territories had adopted legislation that typically prohibited adulteration of a drug "with the effect of weakening or destroying its medicinal power."<sup>32</sup>

The first general federal statute regulating the quality of drugs was the Pure Food and Drugs Act of 1906, passed on June 30 of that year. 34 Stat. 768. The Act prohibited the misbranding and adulteration of drugs. The first major challenge to the Act involved a number of drugs, including "Cancerine tablets," that were offered as "Dr. Johnson's Mild Combination Treatment for Cancer, Tumor and Other Chronic Diseases." *United States v. Johnson*, 177 Fed. 313 (W.D. Mo. 1910). The district court dismissed an

<sup>28</sup> *Id.* at 101, n.17.

<sup>29</sup> *Ibid.*

<sup>30</sup> *Adulteration of Drugs*, 15 Am. J. Pharm. 382-383 (1849), cited in Blake, *supra*, note 27, at 102, n.19.

<sup>31</sup> Blake, *supra* note 27, at 106.

<sup>32</sup> Blake, *supra* note 27, at 106-107.

indictment alleging that Dr. Johnson had misbranded the drugs because they were not effective in the treatment of cancer. This Court affirmed on the ground that Congress had only sought to prohibit misleading statements made with respect to a drug's ingredients, not with respect to its effectiveness. *United States v. Johnson*, 221 U.S. 488 (1911). Congress reacted the next year, 1912, by passing the "Sherley Amendment," 37 Stat. 416, which defined the term "misbranded" so as to include any statement "regarding the curative or therapeutic effect of such article \* \* \* which is false and fraudulent."

Twentieth-century history of federal regulation of drugs is in large measure the history of a contest between the promotion of unproven remedies for common, serious diseases and the law's demand that therapeutic claims be proved. Beginning in 1908 the FDA's annual reports reflect a continuing concern about remedies promoted fraudulently as "a panacea" for diseases, and about supposed remedies that lead purchasers to "lose valuable time which could be employed to advantage by resorting to" proper treatment.<sup>33</sup>

<sup>33</sup> See P. Dunbar, *Federal Food, Drug, and Cosmetic Law Administrative Reports 1907-1949* 58 (1951) [hereinafter cited as Dunbar]. In 1911 the FDA again noted that reliance on "so-called 'cancer cures' \* \* \* may cause the loss of invaluable time" in the treatment of the condition. *Id.* at 224-225 (characterizing false cancer remedies as "a definite public health menace"). The 1930 FDA Report stated that such remedies may not only harm the user but "cause delay in resorting to rational methods of treatment." *Id.* at 723. This

Cancer is among the diseases most frequently claimed as being curable in a simple, painless way by a new or rediscovered method of treatment.<sup>34</sup> These asserted cures have included "Radol," claimed to be radioactive water, but actually ordinary water;<sup>35</sup> cloth bags consisting of sand and boneblack, which absorb "cancer poison;"<sup>36</sup> a paste made from lim-

concern was reiterated in the annual reports for 1931, 1942-1943, and 1947, when at least one death was attributed to misguided reliance on a fraudulent cure. *Id.* at 753-754, 1060, 1298. In 1950, the FDA noted that the "search for a 'magic cure' still persists among the gullible, hypochondriacs, and sufferers of chronic ailments \* \* \*," and that worthless preparations, including cancer remedies, have "dangerous possibilities of causing irreparable harm." FDA, *Annual Reports 1950-1974* 16 [hereinafter cited as *Annual Reports (1950-1974)*]. A public warning was issued in 1956 (*id.* at 178), and educational programs against cancer quackery were undertaken in 1958. *Id.* at 224. In 1961 and 1962 the FDA and the American Medical Association sponsored national educational programs on quackery, which was estimated at that time to cost consumers more than one billion dollars annually. *Id.* at 339-340. But in 1963 the FDA lamented that "[c]ancer quackery continues to be a major concern" (*id.* at 411), particularly among older citizens who require proper dietary and medical attention but are "often victims of charlatans and quacks." *Id.* at 439.

<sup>34</sup> Fraudulent cancer cures have been discussed in numerous FDA Annual Reports since 1909. See, e.g., Dunbar, *supra* note 33, at 98, 118, 154-155, 312, 631, 771, 745, 841, 901, 1011, 1171, 1227, 1298, 1408-1410; and *Annual Reports (1950-1974)*, *supra* note 33, at 16-17, 72-73, 102-103, 156, 200, 247, 317, 363, 411-413, 471-472, 519, 575.

<sup>35</sup> Dunbar, *supra* note 33, at 101.

<sup>36</sup> *Id.* at 154.



burger cheese and glycerin;<sup>37</sup> a liniment of turpentine, oil, mustard oil, eggs and ammonia;<sup>38</sup> a machine housing colored floodlamps;<sup>39</sup> peatmoss;<sup>40</sup> the "Fountain of Youth," a mixture of spices, oil and suet;<sup>41</sup> a diagnostic kit used to analyze urine;<sup>42</sup> a machine delivering special electronic frequencies;<sup>43</sup> and mineral tablets.<sup>44</sup> A cancer treatment similar in theory to Laetrile was promoted in 1956 by a "nutritional expert" who claimed that cancer is a deficiency disease that can be cured by the use of certain natural vitamins which he, of course, sold.<sup>45</sup> The first seizure of Laetrile was made four years later, on December 28, 1960.<sup>46</sup>

Cancer is, of course, not the only disease for which ineffective cures are promoted. The FDA's annual reports frequently discuss fraudulent remedies for,

<sup>37</sup> *Id.* at 224.

<sup>38</sup> *Id.* at 745.

<sup>39</sup> *Id.* at 1170-1171, 1229, 1298-1299.

<sup>40</sup> *Id.* at 1408.

<sup>41</sup> *Annual Reports (1950-1974)*, *supra* note 33, at 45.

<sup>42</sup> *Id.* at 102.

<sup>43</sup> *Id.* at 317.

<sup>44</sup> *Id.* at 464.

<sup>45</sup> *Id.* at 200-201.

<sup>46</sup> *United States v. An Article of Drug . . . Laetrile (Formula L) etc.* (N.D. Tex., Feb. 7, 1961), D.D.N.J. No. 6543 (June 1962).

among other conditions, consumption (tuberculosis),<sup>47</sup> epilepsy,<sup>48</sup> diabetes,<sup>49</sup> arthritis,<sup>50</sup> and obesity.<sup>51</sup> The list is practically endless; it is, in large measure, the function of an available market. Polio cures evaporated with the advent of the new vaccines.<sup>52</sup> A similar fate befell pneumonia cures when broad spectrum antibiotics were introduced in the 1940's.<sup>53</sup> Until there is a general and certain cure for cancer, that disease will continue to invite the promotion of ineffective remedies.

<sup>47</sup> Dunbar, *supra* note 33, at 58, 98, 152, 155, 312, 368, 606, 631, 664, 692, 711, 797-798, 820, 841, 864, 1011, 1062, 1107, 1165, 1298, 1409; *Annual Reports (1950-1974)*, *supra* note 33, at 17, 130, 176, 200, 247, 317.

<sup>48</sup> Dunbar, *supra* note 33, at 155, 224, 368, 1363; *Annual Reports*, *supra* note 33, at 131, 176, 472.

<sup>49</sup> Dunbar, *supra* note 33, at 606, 693, 754, 767, 797, 864, 1004, 1060, 1062, 1107, 1166, 1225, 1298, 1359, 1410; *Annual Reports (1950-1974)*, *supra* note 33, at 18, 73, 104, 131, 156, 176, 200, 225, 247, 277, 363, 519.

<sup>50</sup> Dunbar, *supra* note 33, at 1011, 1060, 1107, 1296, 1362, 1411; *Annual Reports (1950-1974)*, *supra* note 33, at 16, 46, 75, 179, 204, 224, 247, 277, 316, 363, 413, 470, 519, 555.

<sup>51</sup> Dunbar, *supra* note 33, at 631, 693, 711, 1297; *Annual Reports (1950-1974)*, *supra* note 33, at 103, 276, 414, 519.

<sup>52</sup> They appear to have flourished until the early 1960's. See *Annual Reports (1950-1974)*, *supra* note 33, at 104, 200, 317.

<sup>53</sup> See *e.g.*, Dunbar, *supra* note 33, at 631, 664, 745, 770, 864, 893, 1108.

FOR ARGUMENT

Supreme Court, U. S.  
FILED

APR 10 1979

ROSAK, JR., CLERK

In the Supreme Court of the United States

OCTOBER TERM, 1978

No. 78-605

UNITED STATES OF AMERICA, ET AL.,  
Petitioners,

VERSUS

GLEN L. RUTHERFORD, ET AL.,  
Respondents.

On Writ of Certiorari to the United States  
Court of Appeals for the Tenth Circuit

BRIEF OF RESPONDENTS

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In the  
Supreme Court of the United States

OCTOBER TERM, 1978

No. 78-605

UNITED STATES OF AMERICA, ET AL.,  
*Petitioners,*

V E R S U S

GLEN L. RUTHERFORD, ET AL.,  
*Respondents.*

On Writ of Certiorari to the United States  
Court of Appeals for the Tenth Circuit

**RESPONDENTS' BRIEF**

**OPINIONS BELOW**

The opinion of the court of appeals (Pet. App. 1a-7a) is reported at 582 F.2d 1234. The opinion of the district court (Pet. App. 11a-44a) is reported at 438 F.Supp. 1287. The decision of the Commissioner of Food and Drugs (Pet. App. 45a-274a) is reported at 42 Fed. Reg. 39768.

**JURISDICTION**

The judgment of the court of appeals (Pet. App. 8a-9a) was entered on July 10, 1978. On August 4, 1978, the court of appeals denied a Motion for Clarification or in the alternative Petition for Re-Hearing filed by respondents (Pet. App. 10a). The Petition for a Writ of Certiorari was filed on October 10, 1978, and granted on January 22, 1979. The jurisdiction of this Court rests on 28 U.S.C. 1254(1).



### QUESTIONS PRESENTED

1. Whether the safety and effectiveness requirements of the Federal Food, Drug, and Cosmetic Act apply to terminally ill cancer patients desirous of taking Laetrile.
2. Whether Laetrile is exempt from the pre-market clearance requirements of the Federal Food, Drug, and Cosmetic Act by operation of the transitional provisions of the 1962 amendments to the Act (generally referred to as the 1962 grandfather clause).
3. Whether the Food and Drug Administration prohibition of the use of Laetrile by a class of terminally ill cancer patients violates those patients' Constitutionally guaranteed right of privacy.

### CONSTITUTIONAL AND STATUTORY PROVISIONS INVOLVED

1. Amendment I to the United States Constitution.
2. Amendment IV to the United States Constitution.
3. Amendment V to the United States Constitution.
4. Amendment IX to the United States Constitution.
5. Amendment XIV to the United States Constitution.
6. 21 U.S.C.A., Section 321(g)(1):

"The term 'drug' means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or preven-

tion of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clauses (A), (B), or (C) of this paragraph; but does not include devices or their components, parts, or accessories."

7. 21 U.S.C.A., Section 321(p), provides in pertinent part:

"The term 'new drug' means—

(1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof,"

8. Section 107(c)(4) of the Drug Amendments of 1962, Pub. L. No. 87-781 (76 Stat. 789) (1962 grandfather clause) provides:

"In the case of any drug which, on the day immediately preceding the enactment date [October 10, 1962] (A) was commercially used or sold in the United States, (B) was not a new drug as defined by Section 201(p) of the basic Act as then in force [21 U.S.C.A. 321(p)] and (C) was not covered by an effective [new drug] application under Section 505 of that [Act 21 U.S.C. 355], the amendments to Section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day."

9. 5 U.S.C.A., Section 706, Scope of review:

"To the extent necessary to decision and when presented, the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall—

- (1) compel agency action unlawfully withheld or unreasonably delayed; and
- (2) hold unlawful and set aside agency action, findings, and conclusions found to be—
  - (A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law;
  - (B) contrary to constitutional right, power, privilege, or immunity;
  - (C) in excess of statutory jurisdiction, authority, or limitations, or short of statutory right;
  - (D) without observance of procedure required by law;
  - (E) unsupported by substantial evidence in a case subject to sections 556 and 557 of this title or otherwise reviewed on the record of an agency hearing provided by statute; or
  - (F) unwarranted by the facts to the extent that the facts are subject to trial de novo by the reviewing court.

In making the foregoing determinations, the court shall review the whole record or those parts of it cited by a party, and due account shall be taken of the rule of prejudicial error."

**STATEMENT**

This action was instituted by cancer patients on March 12, 1975, seeking to enjoin the Government from interfering with the sale and distribution of **Laetrile** for the personal use of individual cancer patients. In August, 1975, the district court issued a preliminary injunction enjoining the Government from preventing the purchase and interstate transportation of a limited quantity of Laetrile for the personal use of Glen L. Rutherford.

The decision granting this preliminary injunction was appealed by the Government to the Tenth Circuit Court of Appeals, which upheld the injunction but reached the conclusion that the Federal Food and Drug Administration most probably had not developed a sufficient administrative record on the subject of Laetrile to properly formulate its opinion that Laetrile was a "new drug." Therefore, the court of appeals ordered the district court to remand the case to the Food and Drug Administration for proper proceedings if a determination was made that the Food and Drug Administration had not developed a proper administrative record.

At a hearing held on December 30, 1976, the district court determined that a competent administrative record did not exist and then in response to the court's request that the FDA make available the written basis of the agency's determination with regard to Laetrile, no matter how casual or unstructured its form or content might be, the court was advised that no such rationale existed in any form. Based upon the lack of an administrative record the district court remanded the action to the Food and Drug Administration for proper administrative proceedings.

On remand to the Food and Drug Administration, an administrative proceeding of sorts was conducted with the Commissioner finally concluding as follows:

- (a) That Laetrile is a "drug."
- (b) That Laetrile is a "new drug."
- (c) That Laetrile does not satisfy the pre-marketing approval requirements for new drugs.
- (d) That there is an absence of scientifically sound data upon which experts could base an opinion that Laetrile is safe for use in man.
- (e) That Laetrile did not meet the statutory criteria of either the 1938 or 1962 grandfather exemptions.
- (f) That Laetrile is not safe and effective.

Respondents sought judicial review of the Commissioner's decision before the Honorable Judge Luther Bohanon. Judge Bohanon vacated and set aside the agency decision and issued an injunctive order exempting Laetrile from the new drug requirements.

The district court sustained the portions of the Commissioner's conclusion that Laetrile is not generally recognized as safe and effective but determined that Laetrile would be exempt from the Act's pre-market approval requirements by virtue of an exclusion under the 1962 grandfather clause. The court further concluded that to deny respondents' use of a non-toxic substance in connection with their own personal health care offended the constitu-

tional right of privacy and, therefore, ruled that it would be unconstitutional to deny the use of Laetrile to a "terminal" cancer patient.

The Government appealed this decision to the Tenth Circuit Court of Appeals which declined to rule on either the 1962 "grandfather clause" exemption or the constitutional right to privacy relied upon by the lower court. Instead, the Tenth Circuit ruled that the "safety" and "effectiveness" requirements of the statute have no application to terminally ill cancer patients who desire to take Laetrile intravenously.

The Tenth Circuit Court of Appeals entered its order holding that the lower court's permanent injunction should be continued but limited to procurement of intravenous injections administered by a licensed medical practitioner to persons certified to be terminally ill of cancer in some form. The court then remanded the case to the lower court for further proceedings consistent with its findings. The court noted that it was "confident that the FDA with all care and due dispatch will promulgate regulations within the above limitations and as if the drug was found by the Commission to be 'safe' and 'effective'" for the limited group considered.

The decision of the Tenth Circuit Court of Appeals was appealed to the United States Supreme Court. Certiorari was granted on January 22, 1979.



### SUMMARY OF ARGUMENT

Initially, it is of great import to define clearly the parameters of the lower courts' opinions.

Neither the opinion of the district court nor the Tenth Circuit Court of Appeals purports to overrule or even challenge the Federal Food, Drug, and Cosmetic Act. Rather, both opinions apply solely to the ruling of the Commissioner relative to Laetrile.

At this point in the litigation the lower courts' exclusion of Laetrile from the Federal Food, Drug, and Cosmetic Act is inherently restricted by the following requirements:

- "(1) The rulings apply only to Laetrile.
- (2) The rulings apply only to usage of the liquid form of Laetrile.
- (3) The rulings apply only to terminal patients.
- (4) The rulings apply only to cancer patients.
- (5) The rulings apply only to Laetrile as it is administered by a qualified practitioner."

(1) The Commissioner has taken the unchanging and dogmatic opinion that no exemption for "terminally ill cancer patients" is found within the Federal Food, Drug, and Cosmetic Act and, therefore, no matter what the evidence is, such exception will not be found. The Federal Food, Drug, and Cosmetic Act as well as being subject to enforcement by the Food and Drug Administration is also subject to judicial interpretation. *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609 (1973).

Notwithstanding the Government's argument that the term "terminal" is difficult of definition, it is a term which is used by medical practitioners on a daily basis and which has a well defined meaning within the medical profession. The only variation implicit in the term is the time frame within which the terminal illness will eventually result in death. As to "terminal cancer patients" an application of the Act's requirements of "efficacy" would lead to an absurd result and, therefore, the Act should be held inapplicable to such patients. *Trans Alaska Pipeline Rate Case*, 436 U.S. 631, 643 (1978).

The term "terminal" connotes a state of being for an individual which is inconsistent with "effective" remedies. The word "terminal" by its very definition precludes the existence of approved effective drugs else the patient would not be so classified.

The term "safe" although having some meaning to the plaintiff class of terminally ill cancer patients could only be construed to have a meaning very much removed from the meaning sought to be applied by the Food and Drug Administration.<sup>1</sup>

<sup>1</sup> In this regard it should be observed that the FDA recognizes and approves the use of cancer drugs which admittedly have a potential for great harm to the cancer patient and which in some instances admittedly cause cancer as a side effect. The Physician's Desk Reference, 33rd Ed., 1979, which is a compilation of FDA approved labeling, contains the following listed drugs and the expected side effects.

CYTOXAN (Mead Johnson & Co.) — A dangerous drug which can cause death. This FDA-approved "anticancer" drug actually can also cause cancer, namely secondary malignancies. According to the FDA-approved "safety" data: "the possibility of secondary malignancy, based on available data, should be considered in any benefit-to-risk assessment for the use of the drug." In addition to causing cancer

Not even the Food and Drug Administration asserts that a drug to be "safe" cannot have certain side effects (Brief on the Merits for the United States, p. 17):

"A drug is 'unsafe' for such patients as for anyone else, if it poses risks of shortening life expectancy or aggravating symptoms that are not outweighed by potential benefits of prolonging life, improving health, or ameliorating pain."

With the above definitional limitations in mind the ruling by the District Court for the Western District of Oklahoma which was affirmed with modification by the Tenth Circuit Court of Appeals, was correct in finding lack of applicability of the terms "safe" and "effective" to a class of terminally ill cancer patients.

(2) Laetrile is not subject to the "effectiveness" requirements of the Federal Food, Drug and Cosmetic Act by virtue of its exclusion from such requirements by the 1962 "grandfather clause." The district court examined the administrative record and, after finding that the adminis-

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<sup>1</sup> (Continued)

and death, numerous side-effects can occur from this drug, including destruction of immune systems, leukopenia, hemorrhage, gonadal suppression, resulting in amenorrhea or azoospermia, possibly "irreversible." The drug is not represented to be cancer-curative.

ADRIAMYCIN (Adria Laboratories, Inc.) — The FDA-approved data on "safety" states that special attention "must be given to the cardiac toxicity" exhibited by this drug. Such labeling data further states that "Congestive heart failure and/or cardiomyopathy may be encountered several weeks after discontinuation" of therapy with this drug, and that cardiac failure is often "not favorably affected by presently known medical or physical therapy for cardiac support." According to such labeling, there is a "high incidence of bone marrow depression" and administration of the drug "may result in superinfection or hemorrhage." Numerous severe and body-damaging ad-

trative proceeding was not conducted properly, further concluded that Laetrile was exempt by virtue of the 1962 grandfather clause.

Laetrile meets each and every requirement of the grandfather clause. Laetrile and Amygdalin are chemically identical and the evidence of record establishes that Laetrile was commercially available prior to October 10, 1962. During the time frame prior to 1962, Laetrile was generally recognized by experts as safe for its intended use. Labeling for Laetrile is the same as that utilized prior to 1962. Laetrile was not covered by an effective NDA under the 1938 Act.

The district court's examination of the administrative record and its opinion setting aside said administrative findings is well supported in the law. Although the FDA possesses initial jurisdiction to determine whether a substance is a "new drug" within the Act's meaning, such determination is reviewable by the district court under the Administrative Procedure Act, 5 U.S.C., Sec. 701, *et seq.* The

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<sup>1</sup> (Continued)

verse reactions are also listed in the approved labeling, including acute nausea and vomiting, phlebosclerosis, severe cellulitis, vesication and tissue necrosis (death), fever, chills and anaphylaxis. The drug is not stated to be cancer-curative.

ADRUCIL (Adria Laboratories, Inc.) — According to the manufacturer's FDA-approved "safety" data, this is a "highly toxic drug with a narrow margin of safety." It is further stated that "severe hematologic toxicity, gastro-intestinal hemorrhage, and even death may result" from use of this drug, despite "meticulous selection of patients and careful adjustment of dosage." "Myelosuppression" (bone marrow suppression, particularly spinal) "almost uniformly accompanies a course of adequate therapy" with this drug, according to the aforesaid approved FDA labeling. Other and severe dangerous effects are also described in such labeling.

district court, after examining the administrative proceedings; the record compiled; and the Commissioner's decision (42 Fed. Reg. 39768-398806 (1977)) found the Administrator's decision to be arbitrary, capricious, representing an abuse of discretion and not in accordance with the law.

The Administrative Procedure Act and the appeal provisions provided therein were promulgated by a Congress which realized that, in many instances, an administrative agency has special expertise in its area of control and, therefore, should be given initial opportunity to conduct proper proceedings. Nonetheless, Congress deemed it appropriate, within our legal system, to provide for judicial review of the individual agencies' administrative findings. The FDA has had every opportunity to prepare an adequate record substantiating its longstanding opposition to Laetrile and the court's finding that the FDA failed to do so was made properly within the context of the existing framework for review.

(3) The district court's determination that a denial of the use of Laetrile by terminal cancer patients infringed

<sup>1</sup> (Continued)

**BICNU** (Bristol Laboratories, Division of Bristol Myers Co.)—According to the FDA-approved "safety" data for this drug, "delayed bone marrow toxicity is the major toxicity." Other and serious side effects and adverse reactions are also listed. Additionally, the drug causes cancer, the FDA-approved labeling stating "BICNU is carcinogenic in rats and mice, producing a marked increase in tumor incidence in doses approximating those employed clinically." Alleged "benefits" are stated to be "palliative."

**MITHRACIN** (Manufactured by Pfizer Laboratories for the Dome Division, Miles Laboratories, Inc.) — The FDA-approved "safety" data for this product states: "Severe thrombocytopenia, a hemorrhagic tendency and even death may result from the use of Mithracin." It is further stated that a detailed analysis of the clinical data in 1,160

upon their constitutionally guaranteed right to privacy was cited as a separate and independent basis for the lower courts' decision. The privacy right cited by the court flows from the decisions in *Roe v. Wade*, 410 U.S. 113 (1973) and *Doe v. Bolton*, 410 U.S. 179 (1973). Recognition was given to the intentions of the FDA in protecting the public; however, the court found that said intention was not an overriding issue given the fundamental nature of the individual privacy right involved.

The decision of the district court is particularly pertinent when it is noted that the Food and Drug Administration has full statutory power to combat false or fraudulent advertising of ineffectual or unproven drugs under both the Federal Food, Drug, and Cosmetic Act, Misbranded Drugs and Devices, 21 U.S.C.A., Section 352 (1976); and the Federal Trade Commission Act, Dissemination of False Advertisements, 15 U.S.C.A., Section 52 (1975).

<sup>1</sup> (Continued)

patients treated with the drug "indicates that the hemorrhagic syndrome is dose related." The manufacturer also notes, with FDA approval, that with recommended "doses of 30 mcg/kg/day or less for 10 or fewer doses" there is an "associated drug-related mortality rate of 1.6% (16 patients per 1,000 receiving the drug are killed by the drug, in other words, not their cancer). The FDA-approved death rate from this drug rises to 5.7% (or 57 per 1,000) however, with a higher dosage of "Mithracin" noted in said approved labeling. The approved labeling also designates a veritable host of other dangerous side effects. The drug is not stated to be cancer-curative.

**FLUOROURACIL** (Hoffman LaRoche, Inc.) — The official FDA-approved "safety" labeling in effect as of August 1, 1978 states: "Severe hematological toxicity, gastrointestinal hemorrhage and even death may result from the use of Fluorouracil despite meticulous selection of patients and careful adjustment of dosage." Numerous other adverse and dangerous reactions and side effects are also listed in such official labeling. Alleged "benefits" are stated to be "palliative", only.



In order to overcome the fundamental right of the plaintiff class, the Government must show a compelling government interest.

The Government's statement of its "compelling government interest" is best set out in the Government's Brief in Chief at page 69:

"There is a compelling governmental interest in maintaining a system for the scientific evaluation of the safety and effectiveness of drugs before they are permitted to be marketed."

Thus, the Government's position can best be characterized as asserting the inflexible position that the Federal Food, Drug, and Cosmetic Act, by virtue of interpretation by the Commissioner, requires a certain "system" for the approval of drugs which allows for no exception nor deviation of any kind regardless of the particular circumstances involved. Such dogmatic reasoning, in the face of patent inapplicability of the "effectiveness" requirements to "terminally ill cancer patients" denotes a lack of sound reasoning in tandem with a continuing and irrational opposition to Laetrile which has persisted within the Food and Drug Administration since the 1950's.

Evidence of the Commissioner's unreasoning opposition to Laetrile is best found in the fact that the Food and Drug Administration outlawed Laetrile based upon the fact that it was a "new drug" without even a shred of evidence to establish the "new drug" status. The FDA expressly admitted the lack of any evidence supporting its "new drug" determination even though it had effectively banned Laetrile for many years (App. 42).

As a matter of fact the compelling state interest urged by the Commissioner in the Government's Brief in Chief is nonexistent. None of the lower courts' rulings has overturned any portion of the Federal Food, Drug, and Cosmetic Act. Rather, the controversy surrounding Laetrile has proceeded in an orderly fashion through the courts and the FDA's administrative machinery all in accord with pertinent law.

The FDA made its initial determination that Laetrile was a new drug. This determination was challenged in the United States District Court for the Western District of Oklahoma and was found lacking. On appeal to the Tenth Circuit Court of Appeals the district court's opinion was affirmed but, according to law, it was determined that if the FDA did not have a proper administrative record the case should be remanded to the FDA to allow an administrative record to be prepared. When it was determined that no administrative record existed the case was remanded to the FDA, which then developed its administrative record and issued a decision adverse to Laetrile.

Appeal from the adverse decision of the Commissioner was taken to the United States District Court for the Western District of Oklahoma which overturned the Commissioner's findings. The district court's decision was affirmed by the Tenth Circuit Court of Appeals in an opinion rendered after the Government appealed to that court.

The Commissioner's powers are in no way curtailed by any action taken by any court in this case. Contrary to the Commissioner's assertions in the Government's Brief in Chief, the Food and Drug Administration has had every

opportunity to present its case to the courts and the fact that the decisions have been adverse to the Food and Drug Administration does not imply that the Commissioner's authority has been curtailed. There can be no argument that the Commissioner's decisions are always subject to judicial review of the kind involved in this particular case.

The assertion by the Government that an affirmation of the Tenth Circuit's opinion would inevitably lead to expansion of the usage of drugs unapproved by the Food and Drug Administration is specious. Such expansion would require both administrative and judicial proceedings in line with those held in the instant case and would, therefore, guarantee protection of the public.

(4) Lastly, and probably most importantly, remains the fact that even this Court with its immense power cannot preclude terminal cancer patients from using Laetrile. The original ban on Laetrile led only to the mass exodus of Americans to Mexico and Europe to obtain treatment with Laetrile. Illegal importation of Laetrile by terminal cancer patients then followed inexorably as they returned to the United States with their supplies of Laetrile for continuing treatment. In some cases the ban actually reduced cancer patients to the status of exiles from their own country. Cancer victims who could not morally break the Customs laws by false swearing were forced to remain outside the United States. And, as if the preceding were not bad enough, the ban on Laetrile prior to Judge Bohanon's temporary order resulted in a black market of Laetrile within this country which was not subject to FDA supervision, inspection or testing.

It goes without saying that the same scenario would prevail were a decision adverse to respondents handed down by the Supreme Court. The net effect of a ruling adverse to respondents would be the redevelopment of a black market for Laetrile within this country which would not be subject to scrutiny by the FDA; an exodus of substantial numbers of cancer victims to Mexico and other countries to receive treatment; violation of Customs laws by terminal cancer patients bringing Laetrile back into this country; and an abandonment of their regular family physicians by Americans leaving this country for treatment.

Such results are not at all speculative. They are supported by the facts existing prior to the implementation by Judge Luther Bohanon of an "affidavit system" allowing terminally ill cancer patients to obtain supplies of Laetrile for their own use.

## ARGUMENT

### I.

#### **THE SAFETY AND EFFICACY REQUIREMENTS OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT DO NOT APPLY TO THE PLAINTIFF CLASS OF TERMINALLY ILL CANCER PATIENTS.**

The Tenth Circuit Court of Appeals declined to rule upon the "grandfather clause" issue and the constitutional issue of right to privacy which were the premises for the lower courts' ruling. In lieu of that reasoning the Tenth Circuit ruled that the terms "safe" and "effective" (21 U.S.C., Section 321(p)(1)) do not apply to the use of the intravenous form of Laetrile by the plaintiff class of terminally ill cancer patients when under a doctor's supervision.

No authority was cited by the Tenth Circuit for the above premise other than the logical statement that "safe" and "effective" would have no meaning to a terminal cancer patient who has been told that he is going to die anyway. The court went on to state that there was no applicable or reasonable measure of safety or efficacy against which to test Laetrile.

The court's reasoning is supported by cases cited by the Government. *Trans Alaska Pipeline Rate Case*, 436 U.S. 631, 643 (1978), quoting *Commissioner v. Brown*, 380 U.S. 563, 571 (1965); *United States v. Key*, 397 U.S. 322, 324-325 (1970); *TVA v. Hill*, 437 U.S. 153, 188 (1978).

The cited cases stand for the proposition that a statute may be construed and implied exceptions found if to do

otherwise "would lead to absurd results \* \* \* or would thwart the obvious purpose of the statute" or in order to avoid an obvious inconsistency within the statutory scheme.

To construe the Federal Food, Drug, and Cosmetic Act to require "effectiveness" of a drug intended for use by a patient certified as terminally ill by his physician, would lead to a most patently absurd result. If there were efficacious drugs then there would be no "terminally ill" cancer patients.

Basic to the arguments being presented to the Court by petitioner herein is the "rosy", but totally unjustified "imputation" that with orthodox, or conventional, cancer therapies we are rapidly winning the battle against cancer, and that, therefore, we need look no further to such therapies as those afforded by Laetrile, and its accompanying metabolic therapies as employed by physicians throughout the United States, and over the World. However, the Government's own statements and statistics demonstrate that we are not winning the battle against cancer, but losing it very rapidly, the conventional therapies being totally inadequate to handle the problem.

In 1977, 400,000 Americans died of cancer, a figure which is seven times the total fatalities in the Vietnam and Korean wars. According to Dr. Marvin Schneiderman, Associate Director of the National Cancer Institute, the death rate from all types of cancer is continuing to increase. Dr. Schneiderman also states that cancer mortality, overall, is increasing, so that it is the only major cause of death which has continued to rise from 1900 through



1976. Putting it another way, more people are dying today from cancer in every age group than have died from cancer in such age groups at any other time in American history. According to present projections 1 in 4 Americans is doomed to die of cancer. Pursuant to the best available government statistics, the cancer death rate in 1900 was 64 per 100,000 of the population, a figure which has now increased to 162.8 per 100,000, or almost a three-times increase. As recently as 1965, the cancer death rate per 100,000 persons was only 127.9. Within the overall statistics, there are equally unfavorable figures as to specific types of cancer. For example, between 1973 and 1975, the number of lung cancer cases increased in the United States 13%, and breast cancer, 17%, stomach cancer, 28%, and prostate cancer, 32%, for the same period. Nor is median survival time particularly encouraging for the cancer sufferer. According to the U. S. Department of Health, Education, and Welfare, the observed median survival time in approximately 219,500 cases of cancer (all sites) was 1.7 years. This median survival time includes those cases wherein a cancer is localized, or limited to the site of origin. Of great interest, however, are the statistics concerning distant (disseminated or "metastasized") cancer, wherein the U. S. Government has stated that the five-year relative survival rate ranges from a maximum of 17% for prostate cancer, to 14% for corpus uteri cancer, 12% for cervix uteri cancer, 10% for female breast cancer, 8% for ovary cancer, 5% for colon cancer, 4% for rectum and bladder cancer, 2% for stomach cancer, 1% for lung and bronchus cancer, and a "zero" survival rate for pancreas cancer for that period. The overall death rate for

those afflicted by distant or disseminated cancers, after a period of five years, is 91%.<sup>2</sup>

Respondents consider this latter figure to be of particular significance, due to the fact that the respondents, together with thousands of other patients who have availed themselves of Laetrile or amygdalin are "terminal." No conventional therapy is of any avail to prolong their lives beyond the dismal life span shown by the Government's statistics, and which inescapably reflect the inadequacy and inefficacy of conventional cancer therapies.

In this connection the petitioner agency apparently believes that cancer patients should willingly and cheerfully die, rather than have Laetrile. In the Administrative Rule Making Hearing on Laetrile, held by FDA on May 2, 1977, Dr. Samuel C. Klagsbrun participated on behalf of the Agency. (Hrg. transcript, page 60, *et seq.*)

Although a medical doctor, Dr. Klagsbrun does not treat his patients to get them well, but specializes in "helping cancer patients to die." Concerning conventional therapies for cancer, Dr. Klagsbrun stated (page 65): "the odds are slim, we know that, you are not talking to somebody who thinks it is a terrific thing that we have." Nevertheless, Dr. Klagsbrun proudly testified as to successfully

<sup>2</sup> See testimony of Dr. Marvin Schneiderman, Associate Director, National Cancer Institute, March 5, 1979, before Special Subcommittee, U. S. Senate, Edward Kennedy, Chairman; "Facts of Life and Death", U.S. Department of Health, Education and Welfare Publication No. (HRA) 74-1222; "Mortality Trends for Leading Causes of Death", U.S. Department of Health, Education, and Welfare Publication No. (HRA) 74-1853; "Ca-A Cancer Journal for Clinicians"; "Cancer Rates and Risks", 2nd Edition, U.S. Department of Health, Education, and Welfare.

discouraging cancer patients from seeking alternate therapies in Mexico, or elsewhere, and in two instances which he noted had been "successful" in convincing the terminal cancer patient to die rather than opt for an alternative therapy.

This conclusion that cancer patients should willingly die rather than seek alternate therapy lies at the heart of what is involved herein! When a cancer patient is terminally ill from cancer, when orthodox treatments can offer nothing, then the terminal cancer patient has the inalienable right and final choice to choose Dr. Klagsbrun's "success" in dying, or to choose an alternate cancer therapy, involving Laetrile, after informed consent by the administering physician.

The Government cites certain portions of the Congressional proceedings leading to the 1962 efficacy amendments as support for its position that the term "effective" would apply to Laetrile. The Government cites remarks of Senator Kefauver to the effect that the Act would apply to experimental drugs used to treat "cancer in its last stages." 108 Cong. Rec. 17399 (1962). For further support the Government cites comments of Senator Eastland to the effect that "fatal diseases, such as cancer" would be subject to the Act's requirements, noting that approval of such drugs would be appropriate even though they might only prolong life or alleviate suffering. 108 Cong. Rec. 17401 (1962).

It appears that both Kefauver and Eastland were referring to cancer as a disease with a *potentially* fatal propensity. There is nothing in the language cited to indicate

that either Senator was referring to cancer in its "terminal" state.

Nonetheless, Senator Eastland's remarks are particularly helpful in noting that approval of such drugs would be proper if they did no more than prolong life or alleviate suffering.

The administrative record compiled by the FDA is replete with evidence of the "pain-killing" effect of Laetrile.<sup>3</sup>

Neither the Commissioner's findings nor any brief filed by the Government attacks the analgesic effect of Laetrile. In point of fact, the Commissioner's opinion merely notes the fact that claims have been made for the analgesic effect of Laetrile and does not attempt to rebut same. The Commissioner remains content to review affidavits from established medical entities and organizations that Laetrile is not "generally recognized as safe and effective." None of the anti-Laetrile doctors could testify of their own usage of the drug nor of their evaluation of patients who had used the drug to determine if there were an analgesic effect

<sup>3</sup> Laetrile, Administrative Rule Making Hearing, Oral Argument, Carole M. Dunn, pp. 100-108, at 100:

"First, here are the observations of David Rubin, M.D., a surgeon at the Beilison Hospital and a cancer researcher at the Hadasah, Jerusalem, Israel; and Myron N. Issahery, M.D., senior medical consultant to Israel aircraft industries:

"One, with few exceptions all the cases they saw were advanced, incurable cancer patients. Most of them had had conventional therapy before being treated with Laetrile.

"Two, their most striking observation was relief of pain, accompanied by a decrease or even cessation of the need for pain killers and sleeping potions."

See also, the remainder of Ms. Dunn's testimony relative to the analgesic effect of Laetrile, particularly the effect found by Mrs. Dunn in treatment of her own cancer.

which would bring Laetrile within the "effective" classification of the Act as perceived by Senator Eastland.

Thus, even assuming the FDA's own assertion that, the term "effective" has some meaning to terminal cancer patients, Laetrile meets that requirement within the framework established by the Food and Drug Administration.

The determination of the safety of Laetrile as considered by the district court was dismissed by the Government in its Brief in Chief by the following language at 55:

"It was error for the Court to ignore the considered opinions of leading cancer specialists on which the Commissioner relied, and to accept instead the anecdotal experiences of a handful of Laetrile practitioners who themselves are not qualified experts."

<sup>3</sup> (Continued)

Testimony of Norma Manke at 225-226:

"Before going on the program I was unable to get out of bed. I felt so bad I didn't want to live and that was four or five months ago. Today I feel well."

Testimony of Maxine Meyers, pp. 281-289, at 287, in reference to Mrs. Meyers' husband:

"After three months on the FU5, the doctor told us there was nothing more to do and he was sent home from the hospital to die at home. I was told he had only a few days to live.

"Instead, one of my sons and I took him to Mexico to the Delmar Hospital for the Laetrile treatment. He was taken off all drugs and medication except Laetrile and enzymes. Within two days, he was able to get out of bed and walk outside. His appetite returned. His mind cleared. And above all else, the pain went away."

Testimony of Philip E. Binzel, Jr., M.D., 360-364 at 362:

"That nutritional therapy has improved the quality of life, for whatever time there may be left for most of those patients, there can be no doubt."

See also, report of David Rubin, M.D., Administrative Record 510, ex. 12.

Contrary to the allegations of the Commissioner, the district court considered the entire record, not merely anecdotal evidence and in support of its ruling enunciated two extensive footnotes, numbers 23 and 24, which are reproduced (our Footnote 4) hereafter verbatim:<sup>4</sup>

Thus, assuming that the term "safe" has some meaning to terminal cancer patients the administrative record bears sufficient evidence of the safety of Laetrile to amply justify the ruling by the district court and by the Tenth Circuit Court of Appeals.

<sup>4</sup> "[23] In the only laboratory study of record specifically designed to determine the drug's toxicity, it was observed: "Amygdalin, at all doses studied, appears to be completely non-toxic in laboratory mice." Harold W. Manner, Ph.D., Chairman, Department of Biology, Loyola University, Chicago, Illinois (R 262). Of the various controversial tests studying Laetrile's efficacy on animal tumors, none have disclosed toxicity at reasonable dosage levels.

Among the numerous scientists and physicians testifying from first-hand experience with Laetrile and its effect on humans, unanimity exists as to its nontoxicity.

Dr. Phillip Binzel, M.D., graduate of St. Louis University, testified that he has personally given nearly 4,000 intravenous injections of Amygdalin using doses up to 9 grams without any adverse reaction. (Tr. 363)

Daniel S. Martin, M.D., who participated in the same Sloan-Kettering experiments in which Dr. Sugiura detected cancer inhibiting properties in Laetrile, and who disputed Dr. Sugiura's results, nonetheless concluded that there was no doubt that Laetrile was nontoxic, at least if administered parenterally. (Tr. 437)

Charles Gurchot, Ph.D., testified for the record in affidavit form that Amygdalin in liquid and solid form was used prior to 1962 (between 1934 and 1945) by Gurchot, under the supervision of five named medical doctors at the University of California Medical School at San Francisco. This Amygdalin was, according to his statement, administered "on patients intramuscularly and intravenously." He further stated that during this same period Amygdalin was being used to his personal knowledge by approximately a dozen California physicians in their treatment of cancer. Gurchot expressed his belief that Amy-



II.

**LAETRILE IS EXEMPTED FROM THE "EFFECTIVENESS" REQUIREMENTS OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BY VIRTUE OF THE TRANSITIONAL PROVISIONS OF THE 1962 AMENDMENTS TO SAID ACT.**

- A. *The District Court's review of the administrative record and the decision promulgated by the Commissioner of Food and Drugs was well within the scope of review as set out in the Administrative Procedure Act.*

Although the Food and Drug Administration possesses initial jurisdiction to determine whether a substance is a "new drug" within the Act's meaning, *Weinberger v. Hynson, Wescott & Dunning*, 412 U.S. 609, 627 (1973), such determination is properly reviewable by a district court under the Administrative Procedure Act, 5 U.S.C., Section 701, *et seq.*; *Weinberger*, *supra*.

In order to be affirmed the agency decision must not be arbitrary, capricious or abusive of agency discretion.

<sup>4</sup> (Continued)

gdalin was generally recognized by experts as being safe for use in the treatment of cancer on or prior to October 10, 1962. (R 302 at J-206)

Chauncey D. Leake, Ph.D., indicated in his affidavit that he is familiar with Dr. Gurchot's use of Amygdalin in the mid 1930's and 1940's at the University of California Medical School Hospital in San Francisco. He further indicates that physicians and other scientists familiar with Amygdalin recognized it as safe at that time. (R 302 at J-200)

Dr Dean Burk, former head of the Cytochemistry Section, National Cancer Institute, Bethesda, Maryland, after testing Amygdalin on rats, says the substance is "notably less toxic to animal organisms than ordinary diet sugar," and that aspirin tablets are 20 times more toxic than an equivalent amount of Amygdalin. (R 183 at 166F)

"Investigators have found that intravenous doses in excess of 20 grams have been without toxic effect in healthy human subjects, al-

*Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 416 (1971). The court must also consider whether the decision was based upon a consideration of all the relevant factors and whether there has been a clear error of judgment. *Citizens to Preserve Overton Park v. Volpe*, *supra*.

And, the reviewing court has the responsibility "to engage in a substantial inquiry" and "this inquiry into the facts is to be searching and careful." *Ethyl Corp. v. Environmental Protection Agency*, 541 F.2d 1, 35-36 (D.C. Cir. 1976).

The court should intervene where it appears from a combination of danger signals, that the agency really has not taken a "hard look" at the salient problems, and has not genuinely engaged in reasoned decision-making. *Greater Boston Television Corp. v. F. C. C.*, 444 F.2d 841, 851 (D.C. Cir. 1970).

The lower court upon its review of the decision of the Commissioner of Food and Drugs concluded that said

<sup>4</sup> (Continued)

though occasionally a mild hypotensive effect may be observed. Repeatedly, studies have indicated that pure Amygdalin, when administered parenterally is astonishingly devoid of toxic effects." (R 183 at 166F)

Donald C. Thompson, M.D., of Morristown, Tennessee, testified as to his personal experience with administering Laetrile to patients and affirmed the drug's nontoxicity. (R 313)

In his report entitled "Use of Laetrile in the Prevention and Treatment of Cancer," Dr. David Rubin, M.D., surgeon at Beilinson Hospital and cancer researcher at Hadassah Hospital in Jerusalem, Israel, asserts: "Laetrile is nontoxic even in very large injected doses." (R 310, Ex. 12)

As another example of a practicing physician who has extensively used Amygdalin and determined it to be nontoxic, see the letter of

decision was arbitrary, capricious, that it represented an abuse of discretion, and that it was not in accordance with law. The court then set aside and vacated the Commissioner's decision.

The court's decision to set aside the Commissioner's findings is well justified when all the pertinent facts are considered. The court noted in its footnote No. 5 the lack of objectivity of the FDA:

"When this suit was initiated, FDA had declared Laetrile a 'new drug' without ever having constructed an administrative record in support of such designation. See *Rutherford v. United States*, 424 F.Supp. 105 (W.D. Okla. 1977). Ideally, agency decisions and conclusions should flow from a probing and objective analysis of a carefully amassed and encompassing factual record. When ordered on remand to conduct an appropriate investigation, FDA begrudgingly announ-

<sup>4</sup> (Continued)

The Honorable Lawrence P. McDonald, Congressional Representative from Georgia. (R 509 at N265-68)

"Amygdalin (Laetrile) is totally non-toxic systemically, at commonly applied dosages." Hans A. Nieper, M.D., Hannover, West Germany. (R 302 at J-180)

While a doctor's inability to control many variables potentially relevant to curing a disease may impugn the credibility of his perceptions as to a drug's efficacy (*see Weinberger v. Hynson, supra*) his observations as to its toxicity are much more reliable, since the relevant variables are more manageable.

"(Laetrile) is totally nontoxic. Its lethal dose in mice and rats, by injection, is about 25,000 milligrams per kilogram of body weight. It is so nearly nontoxic that in some studies the water, used as a dilutant presents a greater toxicity than the vitamin." *The Journal of Applied Nutrition*, Ernst T. Krebs, Jr. (R 302 at J-187)

"... All the available facts indicate that Amygdalin is essentially non-toxic to laboratory animals and to humans." Raymond Ewell, Ph.D. in chemistry from Princeton, retired professor from the State University of New York at Buffalo. (R 302 at J-196)

ced its intentions to do so and then previous to ever having received the evidence on which its conclusions are ostensibly based, FDA reaffirmed its same, entrenched positions on the salient issues in the case. See "Laetrile—Notice of Administrative Rule Making Hearing," (R 1, 42 Fed. Reg. 10066 (1977)). Understandably, many contributors to the administrative record expressed skepticism concerning the proceedings' fairness."

The FDA, however, was not content to republish its previous position in the administrative record, a further step was taken in publishing and distributing a booklet entitled "Laetrile—The Making of a Myth," a booklet which is highly critical of Laetrile, in the time frame after this case had been remanded to the FDA to make its impartial determination of the status of Laetrile.

The administrative proceeding itself belies an open-minded review by the Food and Drug Administration. The

<sup>4</sup> (Continued)

[<sup>24</sup>] "Among experts qualified by scientific training and experience to evaluate the safety of chemical substances in drugs, it is my information and belief that at least since the 1930's pure amygdalin has been generally recognized as safe for use by human beings either by injection, intravenously or intramuscularly, or by oral intake. For example, pure amygdalin may be administered without adverse effect in amounts of 10 grams per day, orally or 3 grams intravenously to a 150 pound man. . . ." Charles Gurchot, Ph.D. (R 302 at J-211 and 212)

The authoritative publication, *The Dispensatory of the United States* (1950 ed. p. 40) emphasizes that "Amygdalin itself is practically non-toxic . . ." *Synopsis of Materia Medica, Toxicology and Pharmacology*, C. V. Mosby Company, 1944, p. 33, affirms that "the glucoside Amygdalin, given by injection, produces no harmful effects." (R 183 at 166F)

"With 45 years of study and research on the cancer problem, . . . I have found no statements of data on demonstrated, sustained pharmacological harmfulness to human beings of amygdalin at any dosages

Food and Drug Administration has promulgated regulations providing for hearings in the event of referral by court. 21 C.F.R., Sec. 10.60. The hearings provided range from very formal to very informal. The Commissioner of Food and Drugs elected to conduct hearings in the matter of Laetrile under the provisions for the most informal proceedings allowed by law. These informal proceedings resulted in a denial to respondents of the right to cross-examine witnesses and allowed testimony to be given without requiring the administration of an oath. Respondents' attorneys objected to this procedure but the Hearing Examiner elected to proceed nevertheless (Administrative Rule Making Hearing, Oral Argument, pp. 10, 11, 27 and 28).

The FDA's selection of its least formal and, therefore, least probative administrative proceeding is especially indicative of the FDA's lack of objectivity when it is taken

<sup>4</sup> (Continued)

recommended or employed by physicians in the United States and abroad, up to the high level of 200 milligrams per kilogram of body weight per day (equals 15 grams—75 kilogram man-day), administered either orally or parenterally; and, more specifically no such statements by official opponents of the use by humans of amygdalin, including comment in their major publications. Few substances have been so widely investigated regarding non-toxicity and chemical definition as has amygdalin, by pharmacologists and chemists in many countries of the world, for over 125 years. . . . Amygdalin has been known and widely recognized for over one hundred years as nontoxic for man." Dean Burk, Ph.D., from the pamphlet *Vitamin B-17 . . . a Brief on Foods and Vitamins*. (R 302 at J-69 and J-65)

In its 1963 "Report on the Treatment of Cancer with Beta Cyano-genetic Glucosides ('Laetriles')" the only potential danger discerned by the Cancer Advisory Council of the State of California was "that the use of one or more of these substances in early cancer, to the exclusion of conventional treatment might well be dangerous since treatment with acceptable, curative methods (surgery or radiation)

into consideration that the Tenth Circuit Court of Appeals required a hearing which would guarantee cross-examination.

The Tenth Circuit in its Order on Remand held that a hearing pursuant to 5 U.S.C.A., Section 554(c) would be required. *Rutherford v. U.S.*, 542 F.2d 1137 (10th Cir. 1976).

The cited provision, 5 U.S.C.A., Section 554(c), contains a provision that hearings conducted thereunder must be pursuant to provisions of Sections 556 and 557 of the Act. Section 556 of the Act provides under sub-part (d) that:

" . . . a party is entitled to present his case or defense by oral or documentary evidence, to submit rebuttal evidence, and to conduct such cross-examination as may be required for a full and true disclosure of the facts . . . "

<sup>4</sup> (Continued)

would thereby be delayed potentially until such time as metastases were manifest and the cancer might therefore no longer be curable. (R 183 at 246F) No toxicity was reported in the 1953 case study report of the Cancer Commission of California Medical Association.

It is only within the context of FDA's creation of this record that the specter of Laetrile's toxicity has even been raised. The drug's reputation for nontoxicity, even among its opponents, is amply documented. See, for example: "Harmless, but Ineffective Remedies," *The Journal of Pharmaceutical Sciences*, Oct., 1975. (R 180 at 190E) FDA allegations of toxicity appear to be more of an afterthought offered to bolster their other conclusions, rather than a reasoned conclusion based on a detached, impartial view of the record.

While apricot kernels can be poisonous if ingested in very large quantities, such contain enzymes not present in Amygdalin; thus, the toxicity of apricot kernels and Amygdalin are not comparable. Deposition of Raymond Ewell, Ph.D. (R 302 at J-197)"



The FDA denied respondents their right of cross-examination which had been mandated by the Tenth Circuit Court of Appeals and generally carried out the proceedings in such a way as to guarantee that the FDA's position would prevail.

It is no wonder that the district court found the Commissioner's decision to be arbitrary, capricious, representing an abuse of discretion and not in accordance with law.

***B. Laetrile is exempted from the requirements of the Federal Food, Drug, and Cosmetic Act by virtue of the 1962 grandfather clause.***

The burden of establishing that Laetrile is a "new drug" is upon the Food and Drug Administration. The case *Durovic v. Richardson*, 479 F.2d 242 (7th Cir. 1973), contained the following language regarding the meaning of "commercially" available within the grandfather clause exemption:

"We assume since Congress was endeavoring to avoid imposing new burdens on drugs which had already achieved 'recognized' status, and usage thereunder to a material extent and for a material time, that a gloss of openly and readily available and broadly distributed in the ordinary course of business as well as lack of restriction to investigational use was intended."

The court then placed the burden of proof squarely upon the FDA:

"Nevertheless we find it impossible to say, on the record presented, that defendants conclusively established that Kreboizen was not 'commercially used or sold' as of October 9, 1962."

The *Durovic* view is strengthened by the order of the Tenth Circuit Court of Appeals upon its remand of the case to the Food and Drug Administration. *Rutherford v. United States*, 424 F.2d 1137 (10th Cir. 1976):

"To support its determination, the FDA in the case at bar would have to present substantial evidence to support the proposition that Laetrile is not generally recognized among qualified experts as 'safe and effective' and that Laetrile is not grandfathered by either of the exemptions discussed above."

The standard by which the district court was required to examine the administrative record is found in the case *United States v. Seven Cartons, More or Less, etc.*, 293 F.Supp. 660 (S.D. Ill. 1968):

"It could be expected that genuinely honest differences in expert opinion on the safety and effectiveness might exist with reference to most drug compounds.

"When such genuine differences of expert opinion addressed to the relevant factual question are expressed in opposed affidavits, the case is not a proper case for summary judgment. That conflict of opinion seems to present a genuine issue of fact for trial.

"The government argues that the rule stated in *Merritt* and subsequent cases is compelled by the state's purpose of protection of the public health. The court does not agree. The statutory purpose is served by an orderly judicial procedure. It cannot justify the decision of factual issues by summary judgment. Where, as here, each party has submitted affidavits in support of its position the court must examine those affidavits to determine whether a genuine difference of expert opinion is presented. If such difference of opinion appears, decision must abide the results of a trial on the issues."

In this case, United States District Judge Bohanon acted as both the trier of fact and law. It then became his prerogative to examine the opposing affidavits and materials in the administrative record and make his determination based upon them.

Thus, with affidavits and other supporting materials asserted by both the petitioners and respondents on the issue of general recognition as safe and effective, the district court acting as the trier of law properly reviewed the materials and set aside the Commissioner's decision.

In order to qualify as a "grandfathered" drug under the transitional provisions of the 1962 amendments to the Federal Food, Drug and Cosmetic Act, Section 107(c)(4) of the drug amendments of 1962, Pub. L. No. 87-781 (76 Stat. 789), it is required that the drug was (1) commercially used or sold in the United States on the day immediately preceding the enactment date of October 10, 1962; (2) the drug was not a new drug as defined by 201(p) of the basic Act then in force; and (3) the drug was not covered by an effective new drug application. If the above requirements are met the efficacy amendment will not apply to such drug when it is intended solely for use under conditions prescribed, recommended or suggested in labeling with respect to such drug.

**(1) Laetrile and Amygdalin are synonymous.**

The Commissioner recognized the content of the substance which was the subject of his rule-making proceeding when the first notice of rule making was published, 42 Fed. Reg. 10066 (1977):

"Laetrile is the name of a product whose major component or ingredient is Amygdalin, a substance that occurs naturally in the pits of apricots, peaches, bitter almonds and in other plant material . . . and it has been known, tested and used [as a cancer remedy] for more than twenty-five years. . . ."

The district court found that there was no real question as to the chemical composition of Laetrile. The chemical identity of Laetrile and Amygdalin is documented fully in the opinion of the United States District Court for the Western District of Oklahoma at footnote 17.

In addition to the sources cited by the district court in its determination that Laetrile and Amygdalin are synonymous is the especially compelling admission of the FDA in its January, 1977 publication, "Laetrile—The Making of a Myth" in which the FDA states:

"Laetrile is the chemical Amygdalin, which occurs naturally in the pits of peaches, apricots, and bitter almonds and other plant material."

The illusory distinction the Commissioner asserts between Laetrile and Amygdalin is nothing more than a red herring intended to obfuscate the real issues before the Court.

**(2) Laetrile was commercially used or sold in the United States prior to the enactment of the 1962 amendments to the Federal Food, Drug, and Cosmetic Act.**

The commercial availability of Laetrile prior to 1962 is well documented in the opinion of the United States District Court for the Western District of Oklahoma, footnote 21.

Laetrile was also listed in the 1907 and 1940 Merck Index, an encyclopedia for Chemists, Pharmacists and Physicians. Amygdalin was listed in the 1907 Index at page 63 and in the 1940 Index at page 38.

All drugs listed in the Merck Index are available to Pharmacists and Physicians thus establishing unequivocally that Laetrile was commercially sold prior to the 1962 Amendments to the Food, Drug and Cosmetic Act.

Even the Food and Drug Administration recognizes that Laetrile has been available prior to 1962. During one of the initial proceedings, in which a temporary injunction was granted to Plaintiff Glen Rutherford, on July 18, 1975, the Government's attorney, Mr. Jay Geller represented to the court as follows:

"Mr. Geller: With respect to this particular drug, as the court is probably able to tell from all the materials submitted by Mr. Watts last week, this particular substance has been around for a long time.

The Court: 1820, I think.

Mr. Geller: At least 25 years, that it has been in current vogue . . ."

The district court also noted that the FDA had placed certain restrictions on the commercial availability and use of Laetrile previous to July 29, 1977, the date on which the Administrative Record and Commissioner's decision were filed and that such restrictions were totally unsupported by any Administrative record whatsoever and were therefore, subject to attack as a matter of law.

The court, thus draws attention to the fact that the FDA implemented an illegal ban on Laetrile because its determination was not based on proper administrative proceedings. The FDA then used the fact of its ban to support its position that Laetrile was not commercially used or sold prior to the enactment of the 1962 Amendments. Such action is of itself arbitrary and capricious.

**(3) Laetrile was generally recognized as safe, by experts qualified by experience and training, prior to the 1962 Amendments to the Food, Drug and Cosmetic Act.**

In order for Laetrile to be exempted by the 1962 Amendments to the Food, Drug and Cosmetic Act, it must have been "generally recognized as safe" by qualified experts prior to 1962. *Durovic v. Richardson*, supra, at 250. The court's decision that Laetrile was generally recognized as safe prior to the adoption of the 1962 Amendments is supported by its lengthy footnote 24 set out previously in this brief as footnote 4 at pages 29-31.

The district court comments at footnote 23:

"Among the numerous scientists and physicians testifying from firsthand experience with Laetrile and its effect upon humans, unanimity exists as to its non-toxicity."



In response to the above, the petitioner states at page 46 of its Brief in Chief that there was no such "general recognition of safety," because "Laetrile was not generally known at all to the community of medical experts."

In the first place, there is no "community" of medical experts, anymore than there is "community" of lawyers, teachers, or butchers, speaking in unison, on a given subject.

Whatever the case, no provision whatsoever of the Food, Drug and Cosmetic Act provides that merely because "experts" know nothing of the substance, that this obviates "general recognition" by those who are actually qualified to express an opinion.

The pertinent provisions of the Federal Food, Drug and Cosmetic Act as it was in effect on October 9, 1962, designated a criterion of "general recognition of safety" by "experts qualified by scientific training and *experience*" to evaluate the safety of a substance. Section 201(p) of the Act, 21 U.S.C. (1958 Ed.) 321(p).

It is submitted that the ignorance of the Government's experts regarding the general recognition of safety of Laetrile cannot constitute the required "experience" mandated by the statute, and therefore, only experts having real knowledge of Laetrile can be qualified to express opinions concerning its safety.

Regardless of the validity of the views of the Government's experts, the various testimony and affidavits presented by petitioner and respondent were properly reviewed by the United States District Court for the Western District of Oklahoma under applicable law. *United States*

*v. 41 Cases, More or Less*, 420 F.2d 1126 (5th Cir. 1970), provides the standard of review:

"... disagreement of experts as to the general recognition of a drug as being safe only creates a fact question for the jury, *United States v. Articles of Drug Labeled in Part Quick-O-Ver*, supra at 448."

See also, *United States v. Seven Cartons, More or Less, Etc.*, supra, at 33.

Thus, Judge Bohanon, acting as the trier of fact, determined that the administrative record supported the view that Laetrile was generally recognized as "safe," by experts qualified by training and experience, prior to the adoption of the 1962 Amendments to the Act.

**(4) Laetrile meets the labeling requirements of the 1962 Amendments to the Federal Food, Drug and Cosmetic Act.**

Initially, the district court pointed out that the FDA erred as a matter of law in its assertion that Laetrile cannot escape new drug classification unless it is shown that "it is currently intended *solely* for use under conditions prescribed, recommended or suggested in its labeling on October 9, 1962." The court analogized this situation to that of aspirin, finding that such interpretation of the Act would render all aspirin, regardless of the use, to be subject to classification as a new drug if *any* aspirin were promoted for a use not intended prior to 1962.

Contrary to the findings of the Commissioner of the Food and Drug Administration, the court found that appropriate statutory construction required that Laetrile be

considered exempt from "new drug" status to the extent that it is currently being used for the same purposes and under the same conditions and labeling as on October 9, 1962.

After pointing out the FDA's legal error, the district court goes on to set out the purposes for which Laetrile is not a new drug in footnote 7 of its opinion:

"1962 labeling characterizes Laetrile as a palliative agent for use in 'cancers beyond aid by standard agents,' and warns that 'it is not to be employed to the exclusion of surgery, radiation or similar standard modalities so long as they are indicated.' Affidavit of Robert S. K. Young, Ph.D. (R 201 at H 234). If 'generally recognized as safe' by qualified experts, the '1962 grandfather clause' prevents Laetrile from being classified or treated as a 'new drug' when labeled in substantially the same manner as previous to October 10, 1962. . . ."

**C. Congress did not intend for the "safety" and "efficacy" requirements to apply to the respondent class of terminally ill cancer patients.**

The Kefauver-Harris Amendment to the Federal Food, Drug and Cosmetic Act added, inter alia, the requirement that drugs be "effective" in addition to the requirement that they be safe. 21 U.S.C.A., Section 385.

The legislative history and judicial interpretation of the efficacy requirement reveals that Congress' intent was to provide protection for consumers of prescription drugs from the economic and the physiological consequences of ineffective medication. The imposition of the additional burden on the drug industry was the subject of extensive

discussions and hearings before the Congressional Committees. See, *Hearings on S.1552 before the Senate Subcommittee on Anti Trust and Monopoly of the Committee on the Judiciary*, 87th Cong., 1st Sess.1993 (1962).

The efficacy requirement resulted in the licensing procedure for new drugs becoming prohibitively expensive. Culbert, *Freedom from Cancer*, 114 (1976):

"By 1976, it was generally conceded that to meet the compliance of FDA 'safety' and 'efficacy' guidelines in securing licensing of new 'entities,' no less than ten years of trials both animal and human, nor less than 14 to 15 million dollars in expenditures, nor less than 80 thousand pages of paperwork were needed!"

Drug manufacturers are not in a position to spend the time or money required to obtain an NDA for Laetrile. The drug companies would need the assurance that they could obtain a patent on the substance in order to recoup the monies expended in the testing of Laetrile. No such guarantee exists, primarily because Amygdalin occurs naturally in hundreds of plants and also because the substance is being manufactured in Mexico and other countries at the present time.

Also, it would take a very foolhardy drug company, with the knowledge of the FDA's ongoing opposition to Laetrile, to even initiate the testing procedures necessary to obtain an NDA.

Thus, the Federal Food, Drug and Cosmetic Act is being applied not to the drug manufacturers it was intended to apply to, but to a class of terminally ill cancer patients who cannot conceivably afford the extensive testing that is necessary to obtain an NDA.

The sweeping power asserted by the FDA should not be allowed to deny the use of Laetrile by the respondent class of terminally ill cancer patients within the limitations imposed by the lower courts.

### III.

#### THE FOOD AND DRUG ADMINISTRATION BAN OF LAETRILE DEPRIVES TERMINALLY ILL CANCER PATIENTS OF THEIR CONSTITUTIONALLY GUARANTEED RIGHT OF PRIVACY.

##### A. *The Right to Privacy extends to use, by terminally ill cancer patients, of the substance Laetrile.*

The Right of Privacy was first enunciated by this Court in *Griswold v. Connecticut*, 381 U.S. 471 (1965). The right has been found to emanate from the penumbras of the 1st, 4th, 5th, 9th and 14th Amendments to the Constitution. *Roe v. Wade*, 410 U.S. 113 (1973). The Privacy Right has been recognized as "fundamental." *Griswold v. Connecticut*, *supra*.

The language of Mr. Justice Brandeis in his dissenting opinion in *Olmstead v. United States*, 277 U.S. 438, 478 (1928), remains vital today:

"The makers of our Constitution undertook to secure conditions favorable to the pursuit of happiness. They recognized the significance of man's spiritual nature, his feelings and of his intellect. They knew that only a part of the pain, pleasure and satisfactions of life are to be found in material things. They sought to protect Americans and their beliefs, their thoughts, their emotions and their sensations. They conferred, as against the government, the right to be let alone—The most comprehensive of rights and the right most

valued by civilized men. To protect that right, every unjustifiable intrusion by the government upon the privacy of the individual, whatever the means employed, must be deemed a violation . . ."

In the case *Application of President and Directors of Georgetown College*, 331 F.2d 1010, 1017 (D.C. App. 1964), Mr. Justice Burger, in his dissent, commented upon the applicability of Mr. Justice Brandeis' concept of the Right of Privacy:

"Nothing in this utterance suggests that Justice Brandeis thought an individual possessed these rights only as to sensible beliefs, valid thoughts, reasonable emotions, or well-founded sensations. I suggest that he intended to include a great many foolish, unreasonable, and even absurd ideas which do not conform, such as refusing medical treatment, even at great risk."

The right to refuse any and all medical treatment has been recognized by this Court. *Jacobson v. Massachusetts*, 197 U.S. 11 (1904). This same principle has been affirmed even despite risk of death. *Erickson v. Dilgard*, 252 N.Y.S. 2d 705, 706 (1962). The Court in *Erickson* stated:

"... it is the individual who is the subject of a medical decision who has the final say and that this must necessarily be so in a system of government which gives the greatest possible protection to the individual in the furtherance of his own desires."

To recognize a right to decline medical attention of any kind, while denying a right of terminal cancer patients to utilize the nontoxic substance Laetrile, would create a bizarre anomaly in the law.



The lower courts' decisions allowing intravenous use of Laetrile by terminally ill cancer patients falls within the Right to Privacy previously enunciated by this Court.

This Court has dealt with the privacy right in several recent cases within a health context. *Roe v. Wade*, supra; *Doe v. Bolton*, 410 U.S. 179 (1973); *Griswold v. Connecticut*, supra; and *Eisenstadt v. Baird*, 405 U.S. 438 (1972).

In *Griswold*, this Court held that the state could not ban the use of contraceptives without abridging a couple's right to privacy which underlies a marriage relationship. This Court recognized the Right of Privacy within the general spirit of health care.

*Eisenstadt* upheld the right of a person to distribute contraceptives on grounds that a statute prohibiting distribution to single people violated equal protection by distinguishing between the married and single people. The Court stated at 453:

"If the Right of Privacy means anything, it is the right of the individual, married or single, to be free from unwarranted government intrusion into matters so fundamentally affecting a person as the decision whether to bear or beget a child."

In the landmark case, *Roe v. Wade*, supra, this Court expanded the Right of Privacy to encompass a woman's decision to have an abortion. The Court found that the right to an abortion was a "fundamental" right.

The decision in *Roe*, supra, was based, at least in part, on the health of the mother. *Roe* at 727:

"The detriment that the State would impose upon the pregnant woman by denying this choice altogether is apparent. Specific and direct harm, medically diagnosable even in early pregnancy may be involved. Maternity, or additional offspring, may force upon a woman a distressful life in the future. Psychological harm may be eminent. Mental and physical health may be taxed by child care."

Regardless of the weight given the health factor in *Roe*, the health of the pregnant mother is inextricably involved in the Court's rationale allowing abortions.

In declaring the statutes prohibiting abortion to be unconstitutional this Court balanced that right against what was asserted by many as the Right to Life for the unborn fetus.

Even considering the asserted rights of the unborn fetus this Court did not find them strong enough to deny the mother's right to privacy.

*Doe v. Bolton*, supra, another abortion case handed down by this Court on the same day as *Roe*, also struck down criminal abortion statutes as unconstitutional.

Mr. Justice Douglas in his concurring opinion in *Doe v. Bolton*, 410 U.S. 179, 213 (1973), recognized the fundamental nature of the freedom to care for one's own health:

"Third is the freedom to care for one's health and person, freedom from bodily restraint or compulsion, freedom to walk, stroll or loaf."

Mr. Justice Douglas commented further about the right to health care at page 219:

"The right to seek advice on one's health and the right to place reliance on the physician of one's choice are basic Fourteenth Amendment values. We deal with fundamental rights and liberties, which, as already noted, can be contained or controlled only by discretely drawn legislation that preserves the 'liberty' and regulates only those phases of the problem of compelling legislative concern."

The privacy right includes the privilege of an individual to plan his own affairs, for "outside areas of plainly harmful conduct, every American is left to shape his own life as he thinks best, do what he pleases, go where he pleases." *Kent v. Dulles*, 357 U.S. 116, 126 (1958).

The terminally ill cancer patients involved in this case have heard the death sentence from their own doctors. They have been told that orthodox medicine holds no hope for them and that they are suffering from cancer in its "terminal" state. They are perfectly free to decline treatment of any kind, *Jacobson*, supra. Yet, under the construction of the Food, Drug and Cosmetic Act asserted by the Commissioner, they may not seek hope from the nontoxic substance Laetrile.

Those patients with requisite wealth can avoid illegality by obtaining treatment in countries such as Mexico where the treatment is legal, but this alternative is not available to the poor or the bed-ridden.

The ban of Laetrile by the Food and Drug Administration has resulted in a severe limitation on terminal cancer patients exercise of free judgment in matters directly affecting the quality of their lives. It cannot be asserted that these terminal cancer patients are being granted their

"right to be let alone" as long as they are denied free access to Laetrile.

Further, the Government makes no real argument that the use of Laetrile by terminal cancer patients would, in any way, offend the rationale of *Jacobson*, supra, because there is no intrusion upon the "safety of the general public."

The issue is best framed in the language of the district court wherein Judge Bohanon writes at page 27:

"As a nation, however, historically and continuously, we are irrevocably committed to the principle that the individual must be given maximum latitude in determining his own personal destiny.

"To be insensitive to the very fundamental nature of the civil liberties at issue in this case, and the fact that making the choice, regardless of its correctness, is the sole prerogative of the person whose body is being ravaged, is to display slight understanding of the essence of our free society and its constitutional underpinnings. This is notably true where, as here, there are no simple answers or obvious solutions, uncertainty is pervasive, and even the best efforts leave so much to be desired.

"The final consequences are ultimately borne by those whose bodies are the battleground on which cancer's war is waged. Many perceive the drugs acquisition as a life and death matter, and are understandably frustrated and enraged over attempts by their government to deny them the right to decide for themselves questions of such a personal and grave nature."

The court also notes (fn. 10) that not all members of America's leading institutions are opposed to the use of Laetrile. The court cites the affidavit of C. Chester:

"I have stated before, . . . that if the patient has exhausted the benefits of conventional treatment and does not mind the financial outlay, I see no harm in his taking Amygdalin in the way it has generally been used." Affidavit of C. Chester, Ph.D., Vice President and Associate Director for Administrative and Academic Affairs of the Sloan-Kettering Institute for Cancer Research, New York.

It is also significant that nineteen (19) states have promulgated laws permitting and approving the use of Laetrile.<sup>5</sup>

The compelling nature of the health interest invoked by the respondent class of terminally ill cancer patients falls within the spirit and intent of the privacy cases decided by this Court and the same protection should be granted them.

<sup>5</sup> *Alaska* (See Alaska Statutes 08.64.367); *Arizona* (See A.R.S. 36-2451); *Delaware* (See Del. Code Ann. 16 Section 4901); *Florida* (See F.S.A. 458.24); *Idaho* (See Idaho Code 18-7301A); *Illinois* (See S.H.A. 56½, Section 1801); *Indiana* (See Burns Ind. St. Ann. 16-8-8-1); *Kansas* (See S.B. 505 May 8, 1978); *Louisiana* (See L.S.A.—R.S. 40:676); *Maryland* (See Ann. Code of MD, Art 43 Sec. 133 ch 809); *Nevada* (See Nev. Rev. St. 630.303); *New Hampshire* (See R.S.A. 329:30); *New Jersey* (See N.J.S.A. 24:6F-1); *North Dakota* (See H.B. 1214 eff. July 1, 1979); *Oklahoma* (See 63 Okl. St. Ann. Sec. 2-313); *Oregon* (See Oregon Rev. St. 689.885); *South Dakota* (Bill Number 1287 signed 3/16/79 eff. 7-1-79); *Texas* (See Vernon's Ann. Civ. St. 71 art. 4476-5a.); *Washington* (See R.C.W.A. 70-54.130).

**B. *There is no compelling state interest justifying denial of the use of Laetrile to the respondent class of terminally ill cancer patients.***

In order to justify governmental regulation when a "fundamental right" is involved, there must be a "compelling state interest" and also, the legislative enactments "must be narrowly drawn to express the legitimate state interest at stake." *Roe v. Wade*, supra, at 155.

It is paradoxical that petitioner appears more interested in a potential harm to its "system" of control over drugs than in the issues presented in this case.

The Government argues that the contours of this case are deceptively narrow and that a decision in this case would in effect "cripple" the Food and Drug Administration's ability to administer the Act.

It appears that the Food and Drug Administration is seeking, by painting with very broad strokes, to shore up its indefensible position in this case by asserting across the board applicability to other cases. Such is not the truth.

As pointed out in our summary of argument, the lower courts' decisions have inherent limitations precluding across the board applicability to other drugs. The approval of Laetrile by the lower courts is limited to use by individual terminal cancer patients of the intravenous form of Laetrile under the supervision of a doctor.

Additionally, to apply any decision in this case to other drugs, would require administrative hearings and judicial proceedings as carried out in this case and would, there-



fore, preclude applicability of a decision in this case to other drugs.

The bottom line to the Government's argument in this instance is that the Food and Drug Administration does not want judicial review of its decisions. Instead, it obviously wants a "rubber stamp" on any decision it makes. This is contrary to the law. *Weinberger v. Hynson, Westcott & Dunning*, supra; *Citizens to Preserve Overton Park v. Volpe*, supra; *Greater Boston Television Corp. v. F. C. C.*, supra.

The administrative regulations promulgated by the FDA as asserted by the Commissioner are unyielding. They do not represent regulations which are "narrowly drawn to express only the legitimate state interest at stake."

The application of the "safety" and "efficacy" requirements as enunciated by the Food and Drug Administration is overly broad. As has been argued previously, the term "effective" has little or no significance to a terminal cancer patient and, therefore, its broad and unyielding application to the small class of terminally ill cancer patients violates the principle that the regulation must be "narrowly drawn."

For terminally ill cancer patients to be denied the use of Laetrile because of its asserted inefficacy would, if applied across the board, preclude a terminal cancer patient from the usage of any drug for the reason that there could be no effective drug for a terminal cancer patient.

With ample evidence in the record establishing that Laetrile is safe and nontoxic, the ban of Laetrile based on

its "inefficacy" offends the respondent class of terminally ill cancer patients' constitutional right of privacy.

Two recent and extensive articles have been published regarding the constitutional question involved herein. Milis, *Government Regulation of Health-Care Drugs of Questionable Efficacy*, 14 San Diego L. Rev. 378 (1977); and Block, *Laetrile: Individual Choice for Cancer Patients*, 7 New York University Review of Law and Social Change, 313 (1978). Both articles reach the conclusion that under certain circumstances at least, the right to privacy encompasses the right to use Laetrile.

Mr. Milis does not deal with terminal cancer patients. Rather, he deals with an individual desiring to use Laetrile in conjunction with standard therapy. Even in this context, he concludes as follows:

"If a fundamental right is at stake, the appropriate standard of review is strict scrutiny. Under this standard, the government's interest in health and safety cannot offset the individual's privacy interest when a drug of questionable efficacy is used merely as a supplemental treatment. Therefore, statutes regulating drugs of questionable efficacy should be more narrowly drawn so as not to infringe upon the rights of supplemental users of a drug like Laetrile. Making such drugs available through professionally staffed agencies would satisfy the health care rights of these individuals, while removing the uncertainty and mystery surrounding unapproved health cares. Such an approach would improve the current system by assuring that users of Laetrile-type drugs receive complete and competent medical treatment."

Ms. Block concludes her article as follows:

"The right to choose Laetrile as a form of cancer treatment depends on the degree of constitutional protection given this right. Under the standard of *Griswold* and *Roe*, the Laetrile decision is basic to one's life and is, therefore, protected by the fundamental right of privacy. Once that right has been established as fundamental, state law may infringe on it only insofar as necessary to achieve a compelling state interest. For the cancer patient who is terminally ill, who has tried other treatments, and who has no dependents for whom he would otherwise be providing, the state interests are not sufficiently compelling to justify total proscription of Laetrile. These interests can be served best by narrowly drawn regulations of Laetrile that address specific areas of concern and that vary with the different needs of cancer victims."

The compelling state interest in protecting its "system" asserted by the Food and Drug Administration, simply does not exist in this case. The Government's assertion of harm to the FDA's regulatory scheme is predicated upon mere speculation and appears to be founded in the irrational fear that the Commissioner's powers will in some way be limited. The procedural safeguards, both administrative and judicial, as set out above, will provide ample protection for the Commissioner.

IV.

**THIS COURT SHOULD DISREGARD REFERENCES  
TO PUBLICATIONS AND CASE REPORTS WHICH  
ARE OUTSIDE THE RECORD.**

The Government in its Brief in Chief at footnote 8, refers to reports which appeared after the administrative proceeding and which are not a part of the record for review. The Brief Amicus Curiae of the State of California under its Proposition Three, refers to recent events and medical research which are also outside the record and should be ignored by this Court. *New Haven Inclusion Cases*, 399 U.S. 392 (1970).

That this Court should base its review only upon the record reviewed by the district court and the Tenth Circuit Court of Appeals, is axiomatic within appellate procedure.

Respondents have had no opportunity to examine the materials cited by the Government and the State of California, and obviously no opportunity to cross-examine any witnesses to determine the veracity of their statements.

The State of California goes beyond citing literature when it cites the death of Jo Anne Etta Pye, a California resident who purportedly died of cyanide intoxication (Amicus Brief at 20). Ms. Pye's death has been the subject of no judicial proceedings to the best knowledge of respondents and any commentary about the cause of her death is the rankest of hearsay.

Without attempting to refute any of the unproven allegations regarding the death of Ms. Pye, respondents draw the Court's attention to the affidavit of Dr. John A. Rich-

ardson, which is attached hereto as Appendix A, to show that, at least, there is controversy surrounding the actual cause of death of Ms. Pye.

### CONCLUSION

This Court should affirm the decision of the Tenth Circuit Court of Appeals allowing terminal cancer patients the use of the intravaneous form of Laetrile under a doctor's supervision.

Affirmance is dictated by the premises cited by both the district court and the Tenth Circuit Court of Appeals.

The terms "safe" and "effective" have no meaning, or at least not the meaning asserted by the FDA, to terminally ill cancer patients. Laetrile is exempt from the "efficacy" requirements of the Food, Drug and Cosmetic Act by virtue of the transitional provisions of the 1962 Amendments to the Act. Independent of the above, the lower courts' decisions should be affirmed because to do otherwise would be to violate the constitutionally guaranteed right of privacy of the respondent class of terminally ill cancer patients.

Respectfully submitted,

KENNETH RAY COE, of  
LOONEY, NICHOLS, JOHNSON & HAYES  
219 Couch Drive  
Oklahoma City, Oklahoma 73102  
*Attorney for Respondents*

*of Counsel:*

KIRKPATRICK W. DILLING  
DENNIS M. GRONEK

April, 1979

## APPENDIX 'A'

John A. Richardson, M.D.  
415 Kains Avenue  
Albany, California 94706  
415-527-3020

April 2, 1979

### AFFIDAVIT

Mr. Ken Coe, Attorney  
Looney, Nichols, Johnson & Hayes  
300 Lawyers Building  
219 Couch Drive  
Oklahoma City, Oklahoma 73102

Dear Mr. Coe:

It is now quite apparent from a simple examination of the Emergency Room Laboratory results, from Vesper Memorial Hospital, San Leandro, California, in the case of Mrs. JoAnne Pye, that her death was due to metabolic acidosis which would have responded to the administration of bicarbonate of soda intravenously. Had  $\text{NaHCO}_3$  been given to this patient, she would have been able to sit up and walk out of the hospital.

The basis for this opinion is the fact that in the emergency room her blood PH was 6.4, (normal being 7.4); her  $\text{-HCO}_3$  was 4, (normal being 25). Fifteen minutes later her  $\text{-HCO}_3$  was 2. No where is there evidence that anyone recognized this nor is there evidence that soda bicarb was administered.

Metabolic acidosis does not occur suddenly but takes time to develop and in this case, it would be consistent with the vomiting and diarrhea with which she was afflicted during the entire day of her death.

The point is that had this condition been recognized and treated, Mrs. JoAnne Pye would be alive today and



[APPENDIX]

the speculative argument over the possibility of cyanide intoxication would be of tangential polemics and entirely unrelated.

Please note the attached laboratory record from Vesper Memorial Hospital Emergency Room pertaining to this subject.

Sincerely,

s/ John A. Richardson, M.D.

John A. Richardson, M.D.

[Laboratory Report omitted in printing]

STATE OF CALIFORNIA  
COUNTY OF ALAMEDA

Subscribed and sworn before me this 2nd day of April, 1979.

s/ Janice A. Pruett

Janice A. Pruett, Notary Public

[Official Seal of Janice A. Pruett,  
Notary Public, appears here.]

Supreme Court, U. S.  
FILED

APR 20 1979

MICHAEL ROBAK, JR., CLERK

No. 78-605

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**In the Supreme Court of the United States**

OCTOBER TERM, 1978

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UNITED STATES OF AMERICA, ET AL., PETITIONERS

v.

GLEN L. RUTHERFORD, ET AL.

---

*ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF  
APPEALS FOR THE TENTH CIRCUIT*

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**REPLY BRIEF FOR THE UNITED STATES**

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**WADE H. McCREE, Jr.**

*Solicitor General*

*Department of Justice*

*Washington, D.C. 20530*

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## REPLY BRIEF FOR THE UNITED STATES

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1. After the United States filed its main brief in this case, the Supreme Court of California issued its decision in *People v. Privitera*, Crim. No. 20340, Super. Ct. No. CR-32978 (Mar. 15, 1979). The court sustained, against a right-of-privacy challenge based on both the federal and the state Constitutions, the criminal convictions of four distributors of Laetrile and a physician who had prescribed the drug for cancer patients. The convictions had been obtained under sections of the California Health and Safety Code making it a misdemeanor to sell, deliver, prescribe, or administer any drug or device to be used in the diagnosis, treatment, or cure of cancer if the drug or de-



vice has not been approved either under Section 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 355 ("the Act"), or by a designated state board. Cal. Health & Safety Code § 1707.1 (West 1970), § 1709 (West 1971-1978 Cum. Supp.) The court held that the defendants' "asserted right to obtain drugs of unproven efficacy is *not* encompassed by the right of privacy embodied in either the federal or the state Constitutions." *People v. Privitera, supra*, slip op. 4 (emphasis in original).<sup>1</sup>

2. Respondents attack (Br. 29-32) the decision by the Commissioner of Food and Drugs to conduct informal rulemaking proceedings to develop the record on which to make his determination regarding the status of Laetrile. Respondents claim that the use of such proceedings contravened the initial decision of the Tenth Circuit remanding the case to the Food and Drug Administration for development of an administrative record (A. 40-41), manifested a prejudgment of the issues, and improperly denied respondents a right of cross-examination. Since this case is before the Court on the government's petition, respondents' argument can be offered only as a basis for affirming the judgment of the court of appeals. The argument is not a logical ground for affirming that judgment, and in any event lacks merit.

<sup>1</sup> The California Supreme Court's decision reversed a lower court decision holding the convictions invalid on constitutional grounds. *People v. Privitera*, 141 Cal. Rptr. 764 (Ct. App. 1977). We are lodging with this Court copies of the California Supreme Court's decision (with dissenting opinions) in *Privitera*, and we are sending a copy to counsel for respondents.

The court of appeals, in its decision following the remand to the FDA, recognized the "difficulties in making a record when the proponents of a drug are a group of individuals and not the typical drug manufacturer who conducted extensive laboratory tests and assembled a mass of scientific data" (Pet. App. 4a). The court did not hold the Commissioner's proceeding improper, but accepted it as the basis for judicial review (see Pet. App. 5a). Respondents' attack on the proceeding, instead of providing a basis for sustaining the court's judgment, would presumably require a new remand to the Commissioner.

Moreover, the Commissioner's proceeding was entirely appropriate. It was designed to promote easy and effective public participation and to afford Laetrile proponents ample opportunity to submit data, express their views, comment on previously filed testimony, and ventilate all issues.<sup>2</sup> The lack of an opportunity to cross-examine witnesses—a matter respondents did not raise until May 2, 1977, the day of oral argument before the agency (Tr. 10)—did not prejudice respondents or preclude the making of an adequate record for the Commission<sup>er's</sup> decision. The medi-

<sup>2</sup> Members of the public were invited to submit verified written statements on the "new drug" and grandfather clause issues. 42 Fed. Reg. 10066, 10068 (1977). Copies of all record submissions were made available for public inspection in cities throughout the country. *Id.* at 10069. An opportunity was provided to file verified written replies to filed submissions. *Id.* at 10068. Oral argument was held in Kansas City, Missouri, "a place of central location," in order to "permit broader public participation." *Id.* at 10069. Known Laetrile proponents were specifically invited to participate to the fullest extent in the proceeding. See *id.* at 39768.

cal and scientific questions confronting the Commissioner were not of such a nature that the cross-examination afforded in a more formal adjudicatory proceeding would have illuminated the search for truth. *National Nutritional Foods Association v. Weinberger*, 512 F.2d 688, 700 (2d Cir. 1975); see also *Mathews v. Eldridge*, 424 U.S. 319, 344-345 (1976). In any event, an agency's choice of procedures for making decisions is, in the absence of statutory or constitutional constraints, a matter within its discretion and one not lightly to be seized on as a means of disturbing the agency's decision. *Vermont Yankee Nuclear Power Corp. v. Natural Resources Defense Council, Inc.*, 435 U.S. 519, 524, 542-548 (1978). See also *United States v. Florida East Coast Ry.*, 410 U.S. 224 (1973).<sup>3</sup>

<sup>3</sup> Respondents argue (Br. 37) that the FDA improperly treated Laetrile as a new drug without first conducting an administrative proceeding. Administrative action of the type contemplated by the Administrative Procedure Act, 5 U.S.C. 553 and 554, or by section 701(a) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 371(a), is not a prerequisite to regulatory proceedings under the Federal Food, Drug, and Cosmetic Act. *Ewing v. Mytinger & Casselberry, Inc.*, 339 U.S. 594 (1950). See also *Abbott Laboratories v. Gardner*, 387 U.S. 136, 146-148 (1967). The claimant to a drug seized pursuant to 21 U.S.C. 334 has a right to a judicial hearing, and an importer whose drug shipment is denied admission to this country under 21 U.S.C. 381(a) has a right to an administrative hearing with judicial review. In these proceedings the status of the drug may be determined. It is through such proceedings that the FDA is able to block distribution of unapproved "new drugs," and nothing in the applicable statutes or the Constitution requires the agency to make a formal administrative determination before invoking such proceedings.

3. In their attempt to establish that Laetrile was commercially used or sold in the United States on October 9, 1962, as required by the 1962 grandfather clause (Section 107(c)(4) of the Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 789), respondents note that "amygdalin" was listed in the Merck Index for 1907 and 1940 (Br. 36). Even if it is assumed, contrary to our submission (Main Br. 6-7, 41-43), that amygdalin and Laetrile are the same drug, the 1907 and 1940 volumes of the Merck Index do not prove that Laetrile was commercially available in 1962. Indeed, amygdalin was not listed in the Merck Index for 1952 or for 1960, the only editions published between 1940 and 1962. Moreover, amygdalin was never listed in the Merck Index as a finished pharmaceutical product to be used as a treatment for cancer. The 1940 edition, for instance, listed amygdalin as a powder, not a tablet or injectable drug, and described it as a "rarely" used substitute for hydrocyanic acid; the volume described hydrocyanic acid as a drug used in the treatment of "nervous, irritable coughs; in gastralgia of nervous origin, nervous vomiting, [and] gastric irritability." Merck Index 38, 276 (1940).

Respondents also attack (Br. 39-40) the Commissioner's legal conclusion that Laetrile is not exempt from classification as a new drug unless it is shown that it is currently "intended solely for use under conditions prescribed, recommended, or suggested" in its 1962 labeling (Pet. App. 191a, quoting Section 107(c)(4) of the Drug Amendments of 1962, Pub. L.

No. 87-781, 76 Stat. 789), and that "conditions of use" include "what the drug is recommended for" (*ibid.*). Respondents call this a "legal error" (Br. 40) that would lead to such absurd results as the classification of aspirin as a new drug if anyone should promote it for any use for which it was not recommended in 1962 (*id.* at 39); and they contend that the proper rule is that Laetrile may escape new drug classification "to the extent that it is currently being used for the same purposes and under the same conditions as on October 9, 1926" (*id.* at 40; emphasis in original). Respondents' argument, like the reasoning of the district court on which it relies (Pet. App. 15a-16a n.7), overlooks the fact that, under Section 505 of the Act, 21 U.S.C. 355, drugs are licensed not in general but for marketing by specific individual manufacturers. Thus, in respondents' hypothetical case based on aspirin, only that firm whose aspirin was sold for a new and different use would lose its grandfather exemption and be required to secure pre-marketing approval for the drug. See *USV Pharmaceutical Corp. v. Weinberger*, 412 U.S. 655, 664 (1973). This result reflects sound public policy. Even a familiar drug should not be labeled and promoted for a new use without testing showing that it is effective for that use. Otherwise, patients could be led to forsake effective <sup>after</sup> ~~therapy~~ in favor of ineffective therapy.<sup>4</sup>

<sup>4</sup> Respondents contend (Br. 23) that the record is "replete with evidence of the 'pain-killing' effect of Laetrile" which the Commissioner's opinion does not "rebut." Therefore, they contend (Br. 24), Laetrile comes within "the 'effective' classification of the Act

as perceived by Senator Eastland," a supporter of the 1962 Drug Amendments that imposed an effectiveness requirement to be met by all new drugs before they can be approved for marketing. It is unclear whether respondents mean (1) that the proffered evidence of analgesic effect shows that the drug "will have the effect it purports or is represented to have" for its recommended use (21 U.S.C. 355(d)(5)) and therefore meets one of the requirements for approval of a new drug application, or (2) that Laetrile is "generally recognized" as "effective" for relief of cancer pain by "experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs" (21 U.S.C. 321(p)), and therefore meets one of the criteria for escaping classification as a new drug.

The answer to the first possible argument is that there was no new drug application for Laetrile pending before the Commissioner. The answer to the second possible argument is that the Commissioner applied the proper standards and made an appropriate decision in determining that Laetrile is not generally recognized as effective. Applying the relevant statutory standard as construed by this Court (see *Weinberger v. Bentez Pharmaceuticals, Inc.*, 412 U.S. 645, 652-653 (1973)), the Commissioner rejected as unreliable (Pet. App. 100a-101a, 234a-242a) the kind of evidence on which respondents primarily seek to rely—testimonials by patients and physicians—and gave weight to the testimony of those "qualified by scientific training and experience" (21 U.S.C. 321(p)(1)) to evaluate drug safety and effectiveness. Such experts evaluated claims that Laetrile has an analgesic effect (see *e.g.*, Pet. App. 99a-100a, 130a, 131a, 137a-138a, 139a-140a, 144a-145a). They explained that analgesic effects ascribed by some patients to Laetrile are apparently attributable to factors such as placebo reactions and coincidental cessation of therapies with uncomfortable side effects (*id.* at 99a-100a, 234a-242a). (Belief by some patients that Laetrile relieves pain is understandable in view of studies showing that more than 20 percent of cancer patients experience relief of pain when given an inert medication. Moertel, Ahmann, Taylor and Schwartz, *A Comparative Evaluation of Marketed Analgesic Drugs*, 286 N. Eng. J. Med. 813, 814 (1972).)

On the basis of the entire record, the Commissioner properly found that no adequate and well-controlled clinical investigations were submitted to show that Laetrile is effective for any purpose (Pet. App. 100a), and "that the overwhelming majority of experts in the evaluation of the safety and effectiveness of drugs do not

(Continued)



4. Respondents (Br. 48) and certain amici (e.g., McNaughton Foundation Br. 10-11; Cancer Control Society Br. 5-6) point to the existence of some state laws permitting, in varying degrees, some form of Laetrile traffic and use within the states in question. They suggest that the existence of these laws demonstrates that Laetrile is a safe and effective alternative to accepted treatments for cancer, and therefore that the federal government can have no compelling public health interests in forbidding interstate distribution of the drug. These state laws do not, however, purport to represent scientific judgments that Laetrile is a safe and effective anti-cancer drug; indeed, the legislatures of some of these states have expressly stated that their law is not to be considered an endorsement of the drug's worth. See, e.g., Ind. Code Ann. § 16-8-84-4 (Burns 1977 Cum. Supp.); Wash. Rev. Code § 70.54.130 (West 1977 Cum. Supp.). In any event, the willingness of some states to allow traffic in a drug does not establish that the agency entrusted by Congress with the task of regulating the distribution of drugs in interstate commerce may not properly find reasonable and even compelling reasons for barring such distribution. Cf. Nightengale and Perry, *Marijuana and Heroin by Prescription?*, 241 JAMA 373 (1979).<sup>5</sup>

(Continued)

recognize Laetrile as effective" (*id.* at 154a). He accordingly concluded that Laetrile is not generally recognized as safe and effective "for any therapeutic use" (*id.* at 272a).

<sup>5</sup> Amicus the Cancer Control Society cites (Br. 7) John Stuart Mill's essay *On Liberty* (1859) for the proposition that the government has no legitimate interest in forbidding distribution of

## CONCLUSION

For the foregoing reasons, and for those set forth in our main brief, the judgment of the court of appeals should be reversed.

Respectfully submitted.

*Solicitor General*

WADE H. MCCREE, JR.

APRIL 1979

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Laetrile absent proof of harm to persons other than those who choose to use it. Even assuming that the availability of Laetrile would involve no harm to the families of patients mistakenly diagnosed as terminally ill who might forego accepted therapy that could cure or retard their disease, we doubt that Mill's doctrine should be written into our Constitution as a restriction not only on the Federal Food, Drug, and Cosmetic Act, but on various other laws designed to promote the public health and safety. As one scholar has asked: "If the Constitution does not enact Herbert Spencer's *Social Statics*, does it enact John Stuart Mill's *On Liberty* (1859)?" P. Brest, *Processes of Constitutional Decision-making* 798 (1975). See also H. Hart, *Law, Liberty and Morality* 32-33 (1963); e.g., *Roe v. Wade*, 410 U.S. 113, 154 (1973).

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IN THE  
**Supreme Court of the United States**

October Term 1978

**No. 78-605**

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THE UNITED STATES OF AMERICA, et al.,

*Petitioners,*

*v.*

GLEN L. RUTHERFORD, et al.,

*Respondents.*

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**BRIEF OF AMICUS CURIAE  
THE STATE OF CALIFORNIA  
IN SUPPORT OF PETITIONERS**

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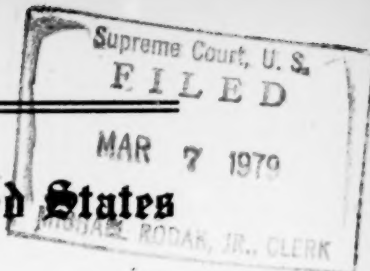
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BRIEF OF AMICUS CURIAE  
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INTEREST OF AMICUS CURIAE

The Attorney General of California is the chief law officer of the state whose duty it is to see that the laws of California are uniformly and adequately enforced. (Cal. Const., art. V, § 13.)

Among these statutes is California Health and Safety Code section 1707.1 which prohibits anyone in California from selling, delivering, giving away or prescribing any drugs, medicine, compound or device for the diagnosis, treatment, alleviation or cure of cancer unless the item has received prior pre-market approval either under section 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355) or by the State of California. In order to obtain approval for the item in question, the basic showing which must be made



according to rigorous scientific proof, is that the item is both safe and effective for the intended use. (Cal. Health & Saf. Code, § 1707.1, subds. (a) - (f); 21 U.S.C. § 355, subd. (d).)

Thus, legal and constitutional significance of the California statute is closely related to the federal statute under consideration in this case. The People of California thus have a vital interest in this Court's resolution of the constitutionality of federal statute 21 U.S.C. section 355 et seq. Therefore, the State of California respectfully submits this amicus curiae brief in support of petitioners, the United States of America, et al.

#### SUMMARY OF ARGUMENT

A requirement that a cancer remedy must first be shown to be both safe and efficacious before being allowed onto the commercial medical marketplace is a valid and necessary exercise of the government's police power. No constitutional right of privacy of a cancer patient is violated by such valid exercise of this police power. Moreover, since laetrile is a potentially dangerous drug, it is particularly appropriate as the subject of governmental pre-market regulations.

#### ARGUMENT

##### I

PREMARKET REQUIREMENTS OF  
DEMONSTRABLE SAFETY AND  
EFFICACY FOR A DRUG IS A  
PROPER AND VITALLY NEEDED  
EXERCISE OF THE GOVERNMENT'S  
POLICE POWER

In repeatedly upholding attacks on premarket requirements of demonstrable safety and efficacy, this Court has made clear that such regulations are a proper and vitally needed exercise of the government's police power. (Weinberger v. Hynson, Westcott & Dunning (1973) 412 U.S. 609, 629-630; Ciba Corp. v. Weinberger (1973) 412 U.S. 640, 654.) Indeed, in interpreting the Federal Food, Drug and Cosmetic Act this Court specifically noted:

"But Congress surely has great leeway in setting standards for releasing on the public, drugs which may well be miracles or, on the other hand, merely easy money-making schemes through use of fraudulent articles labelled in mysterious scientific dress. The standard of 'well controlled investigations' particularized by the regulations is a protective measure designed to ferret out those drugs for which there is no affirmative, reliable evidence of effectiveness. The drug manufacturers have full and precise notice of the evidence they must present to sustain their NDA's [New Drug Applications], and under these circumstances we find FDA hearing regulations unexceptionable on any statutory or constitutional ground." (Weinberger v. Hynson, Westcott & Dunning, supra, at p. 622.)

Such food and drug laws are designed to protect "the public health and pocketbook against adulterated and misbranded drugs" and this objective "has led courts to declare with unanimity that food and drug legislation should be given a liberal construction in order to accomplish its remedial purposes." (United States v. 7 Jugs, etc., of Dr. Salsbury's Rakos (D.Minn. 1944) 53 F.Supp. 746, 752, citing several decisions of this Court.)

Speaking of the Federal Food, Drug and Cosmetic Act of 1938, this Court observed in United States v. Dotterweich (1943) 320 U.S. 277, at page 280,

"The purposes of this legislation . . . touch phases of the lives and health of people which, in the circumstances of modern industrialism, are largely beyond self-protection. Regard for these purposes should infuse construction of the legislation if it is to be treated as a working instrument of government and not merely as a collection of English words. . . ." (Id., emphasis added.)

The Dotterweich case was cited, quoted from and strongly reaffirmed in United States v. Park (1975) 421 U.S. 658, 668-669.) Thus, it is clear that the purpose of these types of premarket authorization as contained in the Food, Drug and Cosmetic Act is to protect consumers who are generally unable to protect themselves. (Kordel v. United States (1948) 335 U.S. 345, 349; Toole v. Richardson-Merrill Inc. (1967) 251 Cal.App.2d 689, 704.) As was stated in Hanson v. United States (D.C.Minn. 1976) 417 F.Supp. 30, 37,

"The history of the Food, Drug and Cosmetic Act in the courts demonstrates that there is no shortage of

peddlers who claim that their miracle drug must be made available to the consuming public without further delay. A parallel history of product liability litigation also demonstrates the danger that new drugs may be released without adequate testing, too often with tragic consequences. The balance between these competing considerations is one which has already been struck by Congress, and it is one which has been repeatedly upheld by the courts. . . ."

It is clear that either the federal government or a state government has broad powers "to establish and enforce standards of conduct within its borders relative to the health of everyone there. It is a vital part of the state's police power. The state's discretion in that field extends naturally to all professions concerned with health." (Barsky v. Board of Regents (1954) 347 U.S. 442, 449.) To justify the use of the police power on behalf of the public it must appear first that the interests of the public require such regulation and second that the means used are reasonably necessary for the accomplishment of the purpose. (Goldblatt v. Hempstead (1962) 369 U.S. 590, 594-595; Lawton v. Steele (1894) 152 U.S. 133, 137.) And, as noted by the California Supreme Court, "A police regulation for the protection of the public health will be sustained if, by any fair construction, it has a tendency to effect its object." (In re Gray (1929) 206 Cal. 497, 502.)

It has been held the interest of the public without question requires the state to regulate both the medical and drug field. "The right to exercise this power is so manifest in the interest of public health and welfare, that it is unnecessary to enter upon

a discussion of it beyond saying that it is too firmly established to be successfully called in question." (Minnesota ex rel. Whipple v. Martinson (1921) 256 U.S. 41, 45.)

Indeed the history of premarket approval requirements for drugs graphically demonstrates that there is a critical need for the government to require such showings of safety and efficacy. Moreover, the methods adopted in the federal statutes are reasonably necessary for the accomplishment of these important goals.

As noted in AMP Incorporated v. Gardner (2d Cir. 1968) 389 F.2d 825, cert. den. 383 U.S. 825, a major medical tragedy led to the passage of the Federal Food, Drug and Cosmetic Act of 1938 and the additions of the "new drug" and "prior approval" provisions. As late as August 1937, the bill was languishing in Congress.

"The bill might well have been enacted without any prior approval sections had it not been for the 'Elixir Sulfanilamide' tragedy of September-October, 1937. [Fn. omitted.] As a direct consequence of that experience, involving the deaths of nearly one hundred persons across the nation who had consumed an untested drug preparation, bills supplementing [the original legislation] . . . were introduced . . . ." (Id., at p. 829.)

As was noted in a report to the Senate on this tragedy, "Most of the drug was administered on physician's prescriptions." (Sen. Doc. 124, 75th Cong., 2d Sess., Nov. 26, 1937.)

By 1962, the public's concern about the impact of drugs or treatments for disease which were not effective prompted President

Kennedy to recommend a hard line to Congress on drug frauds. President Kennedy expressed his concern in a message to Congress recommending strengthening of the existing food and drug laws which resulted in passage of the Drug Amendments of 1962:

"The successful development of more than 9,000 new drugs in the last 25 years has saved countless lives and relieved millions of victims of acute and chronic illnesses. However, new drugs are being placed on the market with no requirement that there be either advance proof that they will be effective in treating the diseases and conditions for which they are recommended or the prompt reporting of adverse reactions. These new drugs present greater hazards as well as greater potential benefits than ever before -- for they are widely used, they are often very potent, and they are promoted by aggressive sales campaigns that may tend to overstate their merits and fail to indicate the risks involved in their use. For example, over 20 percent of the new drugs listed since 1956 in the publication "New and Non-Official Drugs" were found, upon being tested, to be incapable of sustaining one or more of their sponsor's claims regarding their therapeutic effect. There is no way of measuring the needless suffering, the money innocently squandered, and the protraction of illnesses resulting from the use of such ineffective drugs.

"The physician and consumer should have the assurance, from an impartial scientific source, that any drug or therapeutic device on



the market today is safe and effective for its intended use; that it has the strength and quality represented; and that the accompanying promotional material tells the full story -- its bad effects as well as its good. They should be able to identify the drug by a simple, common name in order to avoid confusion and to enable the purchaser to buy the quality drugs he actually needs at the lowest competitive price.

"Existing law gives no such assurance to the consumer -- a fact highlighted by the thorough going investigation led by Senator Kefauver. It is time to give American men, women and children the same protection we have been giving hogs, sheep, and cattle since 1913, under an act forbidding the marketing of worthless serums and other drugs for the treatment of these animals."<sup>1</sup> (1962 U.S. Code Cong. & Admin. News, pp. 4143-4144, emphasis added.)

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1. See Pharmaceutical Manufacturers Ass'n v. Richardson (D.C.-Del. 1970) 318 F.Supp. 301, 307, in which the court cited witnesses before the hearings leading to the 1962 Drug Amendments corroborating President Kennedy's call for impartial judgment on drugs:

"... 'a collection of impressions' will [not] furnish the truth, ... 'this approach did not prevent doctors from having unbounded faith in the curative powers of leeches for hundreds of years before scientific evaluation became the preferred means of judging efficiency of therapy.'

The reasons why Congress followed President Kennedy's message and articulated precise and rigorous scientific standards for proof of compliance with or exemption from the provisions of the 1962 New Drug Amendments is explained in United States v. Articles of Food and Drug, Coli-Trol 80 Med. (D.C.Ga. 1974) 372 F.Supp. 915, 920-921:

"Quite properly, it is simply not enough to show that some people, even experts, have a belief in safety and effectiveness. [Fn. omitted.] A reasonable number of Americans will sincerely attest to the worth of almost any product or even idea. To remove the aberrations in uniformity which can result from a well-staged 'swearing match,' the law requires more. Indeed, it has been heretofore held that the purpose of the normal inquiry is not to determine safety and effectiveness at all, but to ascertain the drug's general reputation in the scientific community for such characteristics. United States v. 41 Cases, More or Less, 420 F.2d 1126 (5th Cir. 1970); AMP, Inc. v. Gardner, 389 F.2d 825 (2nd Cir. 1968), cert. den. 393 U.S. 825, 89 S.Ct. 86, 21 L.Ed.2d 95 (1968). It is certain that a conflicting reputation is insufficient to establish general recognition. United States v. An Article

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1. (Continued)

... '[t]he magnitude of sales of a drug after vigorous promotion is no recommendation for its usefulness or efficacy'; ..."

of Drug--Furestrol Vaginal Suppositories, 294 F.Supp. 1307 (N.S.Ga. 1968), aff'd 415 F.2d 390 (5th Cir. 1969).

"Therefore, what is required is more than belief, even by an expert; it is a general recognition based upon substantial scientific evidence as delineated in the regulatory guidelines. 21 CFR § 130.12. Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609, 619, 93 S.Ct. 2469, 37 L.Ed.2d 207 (1973). There is no reason to differentiate the holding in Hynson between human drugs and animal drugs. United States v. 14 cases--Narengo Medication, 374 F.Supp. 922 (W.D.Mo, Number 2806, January 29, 1974). Public health considerations are similar. Further, logic would dictate no lesser standard after-the-fact than in securing an application. Indeed, the reasoning of the Supreme Court appears to be that 'the reach of scientific inquiry' is the same whatever the forum. Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S. 645(b), 93 S.Ct. 2488, 37 L.Ed.2d 235 (1973)." (Emphasis added.)

The reasons behind a requirement that drugs used in the treatment of cancer be first determined safe and effective were most recently and strongly set forth in the opening remarks of Senator Edward Kennedy, Chairman, Senate Subcommittee on Health and Scientific Research of the Committee on Human Resources at hearings on July 12, 1977, before that Committee on "Evaluation of Information Which the FDA Based Its Decision to Ban the Drug Laetrile from Interstate Commerce," 95th Congress, 1st Session (hereinafter "Hearings"). His remarks are particularly

pertinent to the issues of constitutional protection posed to this Court since he views the laetrile issue not only as a legislator, but also as the father of a child who has cancer, who has committed his child to conventional cancer treatment and who has emerged with his child the apparent victor over his disease:

"There is no disease that the American people fear more than cancer. The very word terrifies many, and conjures up images of pain, suffering and terminal illness. Families fear it when it strikes a loved one because, in some cases, there is so little one can do. There is a feeling of hopelessness and helplessness and, of course, a feeling of guilt.

"I know these feelings first hand. I remember how I felt when the diagnosis was made on my son. What I remember about those first terrible days was the sense of outrage and of injustice that it had happened to him. I remember the search for the cure -- the answer that would save my son's life. I wanted to know every possibility. I wanted to see if there was a special treatment hidden somewhere in the vast array of medical resources available in the country.

"I know how very vulnerable people are in the circumstances -- how willing they are to grasp at any straw -- to try any approach -- to effect a cure.

"This is the time when people need the best information they can get; when they need to be able to

understand realistic alternatives. It is not a time when people are capable of sifting fact from fancy themselves.

"The emotions of the moment make a fully rational choice difficult enough and could tip the balance toward 'quick-fix' panaceas if they were presented as comparable alternatives to proven therapy.

"The role of the Food and Drug Administration in this tragic moment is to guarantee that the available drug therapies are the best and most effective that science can devise. Their role is to protect both the patient and his family from remedies that are neither safe nor effective. The elimination of useless treatments is a valid Federal role. It is a humanitarian role. It reduces the burden on cancer patients and their families and allows them to exercise their freedom of choice on the basis of informed judgments among viable alternatives.

"These issues are brought into dramatic focus by the subject of today's hearing -- Laetrile. Is it a useful addition to the armamentarium against cancer or is it a useless compound which has gained some acceptance because of the vulnerability of the people who decide to use it?

"We all have a high stake in the answers . . . ." (Hearings, at pp. 1-2, emphasis added.)

In dealing with a disease as serious as cancer, the need for prior demonstrations of safety and efficacy are particularly accute.

It is well recognized that the treatment of a life-threatening disease such as cancer with an ineffective drug, is not sound medical practice because any delay in the institution of effective therapy allows the disease to progress unchecked until it may be beyond control. (Durovic v. Richardson (7th Cir. 1973) 479 F.2d 242.) As Justice Douglas stated in Ewing v. Mytinger & Casselberry (1950) 339 U.S. 594, 600:

". . . [Congress] may conclude, as it did here, that public damage may result even from harmless articles if they are allowed to be sold as panaceas for man's ills. . . ."

Indeed, this has been the repeated conclusion of the lower federal courts that have addressed the question. (United States v. General Research Laboratories (C.D. Cal. 1975) 397 F.Supp. 197, 199; United States v. Kordel (7th Cir. 1947) 164 F.2d 913, 917; see also Drown v. United States (9th Cir. 1952) 198 F.2d 999, 1006.)

Thus, given the goals and purposes underlying the premarket requirements of scientifically verifiable proof of both safety and efficacy, it is clear that such regulation is necessary and the means chosen by Congress to achieve that critically important goal are reasonably necessary for the accomplishment of the purpose.



II

ANY RIGHT OF PRIVACY WHICH HAS BEEN DEVELOPED IN RECENT YEARS BY THIS COURT DOES NOT STRETCH SO FAR AS TO ALLOW A PATIENT TO USE THE UNTESTED UNPROVEN DRUG OF HIS CHOICE

Although in recent years this Court has accorded constitutional protection to areas of private decision making in matters relating to family life, such as child rearing and education, procreation, contraceptives, marriage and abortion, none of these cases<sup>2/</sup> support the "right" of a cancer patient to have access to the untested unproven remedy of his or her own choice.

Generally speaking the individual is protected by a zone of privacy which would give him the right to refuse all medical treatment. However, that zone may be entered by the state if there is a compelling state interest at stake. Thus, while an individual may have the right to decide that he will not, as a general matter, accept medical treatment, the state nonetheless can require compulsory small pox vaccination for the compelling state interest of protecting the public from epidemics. (See Jacobson v. Massachusetts (1905) 197 U.S. 11; Muhlenberg Hospital v. Patterson (1974) 320 A.2d 518; Prince v. Massachusetts, supra, 321 U.S. 158, 166-167.)

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2. (Pierce v. Society of Sisters (1925) 268 U.S. 510; Meyer v. Nebraska (1923) 262 U.S. 390; Skinner v. Oklahoma (1942) 316 U.S. 535; Prince v. Massachusetts (1944) 321 U.S. 158; see, e.g., Griswold v. Connecticut (1965) 381 U.S. 479; Eisenstadt v. Baird (1972) 405 U.S. 438; Roe v. Wade (1973) 410 U.S. 113; Doe v. Bolton (1973) 410 U.S. 179.)

But where a patient has made the decision to seek medical treatment venturing into the commercial medical marketplace, he is subject to the valid state regulations of that marketplace. And state regulations in this area need only have a rational relationship to the goal sought to be achieved, i.e., a rational basis. A brief review of the major cases decided by this Court shows the underpinnings of this formulation.

In Griswold v. Connecticut, supra, 381 U.S. 479, the seminal case in this area, this Court struck down a Connecticut statute which prevented a doctor from prescribing to his patients contraceptive devices; devices which were recognized by the medical profession as both safe and effective. (Id., at pp. 481-486.) However, the court specifically noted it was not dealing with a statute that regulated the manufacture or sale of the item but rather the use of that item. Implicit in this discussion was the right of the state to require certain minimum safety and efficacy standards for medical items sold within its boundaries. (Id., at p. 485.)

Later, in Roe v. Wade, supra, 410 U.S. 113, this Court dealt not with the unfettered right of choice of treatment but only with the right of a woman to decide whether to terminate her pregnancy without unwarranted state interference. (Id., at p. 144.) But it must be noted that the Court went on to specifically uphold the right of the state to regulate the entire health care area in which the woman would seek her abortion. (Id., at pp. 163, 173.) Indeed, this Court specifically rejected an argument by some of the amici that an individual had an unlimited right to do with one's body as one pleased which could not in any way be regulated by the state. (Id., at p. 154.) Again, this Court made clear the right to privacy of

the individual did not curtail the more important right of the state to regulate the medical marketplace.

More recently in Whalen v. Roe (1977) 429 U.S. 589, this Court upheld a statute requiring that certain patient-identifying information be provided to the state whenever a physician prescribes a Schedule II drug; drugs in Schedule II (such as opium) have recognized medical uses but the highest potential for abuse among legitimate drugs. (Id., at pp. 592-593 and n. 8.) This Court did not attach constitutional privacy status to the decision to use Schedule II drugs (Id., at pp. 603-604), even though the disclosure requirements might result in patient reluctance to use such drugs when medically indicated. (Id., at p. 600.) This Court held that the disclosure requirements did not constitute "... an invasion of any right or liberty protected by the Fourteenth Amendment," (Id., at pp. 603-604, fn. omitted), and applied a "rational basis" test in sustaining the statute. (Id., at p. 598.)

Some of the appellants in Whalen were doctors who contended that the law impaired their right to practice medicine free of unwarranted state interference. The Court specifically rejected such a sweeping claim of privacy. "We have never carried the Fourth Amendment's interest in privacy as far as the ... appellees would have us. We decline to do so now." (Id., at p. 604, fn. 32.)

Illustrative of the principle that the choice among medical alternatives in the medical marketplace is not itself a decision within the zone of constitutionally protected privacy is this Court's holding in Planned Parenthood of Missouri v. Danforth (1976) 428 U.S. 52. There, this Court struck down a state prohibition of a particular abortion procedure, saline amniocentesis. (Id., at p. 79.) However, the Court did not hold that

the prohibition violated any right to privacy. The Court also did not hold that because the right to privacy encompasses a woman's decision whether to have an abortion, the state therefore may not prohibit a particular abortion procedure. Rather, citing Roe v. Wade, supra, 410 U.S. at page 164, the Court stated the issue before it as follows: "[W]hether the flat prohibition of saline amniocentesis is a restriction which 'reasonably relates to the preservation and protection of maternal health.'" (Planned Parenthood of Missouri v. Danforth, supra, at p. 76, emphasis added.) The Court cited voluminous record evidence of the safety and effectiveness of saline amniocentesis, as compared with other available abortion procedures, and concluded that the state prohibition bore no reasonable relationship to protection of maternal health. (Id., at p. 76.) Significantly, in discussing the validity of the statutory prohibition of this particular medical procedure, the Court did not refer to any constitutional consideration of privacy. No such considerations were involved in the selection of that particular medical procedure by the patient and her physician. The procedure was evaluated by them and by the Court solely on the basis of medical evidence of its safety and effectiveness. (Id., at pp. 75-79.)

Planned Parenthood thus stands for the proposition that although the decision whether to have an abortion is within the constitutional zone of privacy, deserving the protection provided by the "compelling interest" standard, the selection of a particular abortion procedure is a medical matter, to which privacy status does not attach and which may be regulated by government, provided that a rational basis for such regulation exists.

In the instant case, the analogue of the right to decide whether to have an



abortion is the right to decide whether to receive or to forego cancer treatment or to attempt to prevent cancer by the use of drugs. But, although the decision whether to receive any treatment or to attempt to prevent cancer, may be constitutionally protected, the choice among treatment or preventive (if any existed) alternatives is not within the scope of the constitutional right to privacy. No constitutional right is abridged by making available to persons fearful of cancer and to cancer patients only those drugs which are proven safe and effective in cancer prevention or treatment and by precluding the sale or distribution of drugs which are ineffective in preventing or treating cancer.

As was set forth in argument I, supra, the premarket requirements of both safety and efficacy as embodied in 21 U.S.C. § 355 serve the critical need of protecting the public from unproven and thus harmful "remedies." The need for this form of government regulation is so important that it could easily satisfy the "compelling state interest" test used in dealing with fundamental rights. A fortiori, this regulation easily satisfies the rational basis test which properly applies when the state regulates the commercial medical marketplace.

### III

#### RECENT EVENTS AND MEDICAL RESEARCH FURTHER SUPPORT THE FDA COMMISSIONER'S FINDINGS THAT LAETRILE IS NEITHER SAFE NOR EFFICACIOUS

After conducting extensive hearings to develop an administrative record on laetrile, FDA Commissioner Kennedy concluded that laetrile is not generally recognized by qualified experts

as a safe and effective cancer drug. Moreover, he noted that there is frank evidence of toxicity from the ingestion of the kernels or pits of apricots. (42 Fed.Reg. 39806 (Aug. 5, 1977).)

Since the date of those findings further evidence has developed to support his determination.<sup>3/</sup> There is now evidence that laetrile may be mutagenic. (See Science (Nov. 11, 1977) vol. 198, pp. 625-626.) An important retrospective analysis is also now available. The National Cancer Institute undertook a study of individuals who had been using laetrile in this country. Letters were sent to 385,000 physicians and 70,000 other health professionals. Additionally, contact was made with organized pro-laetrile groups. Evaluation of the cases submitted revealed no statistical basis for concluding that laetrile has any anti-cancer activity. The full report of this analysis is reported in Special Report on Laetrile: The NCI Laetrile Review (Sept. 7, 1978) New England Journal of Medicine (vol. 299, no. 10), page 549 et seq.

Additional studies and reports on the inherent toxicity of laetrile when taken orally are also available. They are carefully noted in The Current Status of Laetrile (Sept. 1978) Annals of Internal Medicine (vol. 89, no. 3), page 389 et seq. The authors of the

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3. It is of course true that the general rule of appellate review is that a decision by the court or an administrative agency should be evaluated upon the evidence before that entity at the time of its decision. However, in an area of continuing scientific investigation, such as laetrile, a court should always remain receptive to new scientific data which may have important ramifications on the legal issues under consideration. It is in this framework that amicus curiae presents the material in this argument.



report note, "With oral dosing, a toxic potential is manifest." (Id., at p. 391.) This point was recently brought home by the death of California resident Jo Anne Etta Pye. Mrs. Pye had a history of cancer of the breast but she refused to have any type of surgery or conventional therapy. Mrs. Pye turned to laetrile in oral form. On December 3, 1978, Mrs. Pye died as a result of cyanide intoxication from the laetrile. Moreover, the unchecked cancer had begun to spread through her body. (Amicus curiae respectfully requests that this Court take judicial notice of the records of the Alameda County Coroner, attached to the brief of amicus curiae, the American Cancer Society, as exhibit B. These records fully support the statements made in this argument.)

Mrs. Pye's death graphically illustrate the two fold danger in laetrile. Not only is there the danger from the nature of the drug itself, but also there is the danger of delaying those treatments already proven safe and effective, thereby allowing the disease to spread unchecked.

In United States v. Kordel, supra, 164 F.2d 913, 917, the court stated:

"All were agreed that while the claims were absurd and fantastic, they were dangerous in that they tended to lull people into a false sense of security in reliance on the drugs when they might need professional diagnosis and treatment for conditions which might respond to treatment if correctly diagnosed early enough, but which might become much more serious if not taken care of early. . . ."

Similarly, in a case involving the sale of a device by a chiropractor in violation of the Federal Food, Drug and Cosmetic

Act, the appellant argued that the instrument could not possibly harm anyone. The court responded that:

"While the instruments may be harmless in themselves, their danger lies in the possibility that 'ignorant and gullible persons are likely to rely upon them instead of seeking professional advice for conditions they are represented to relieve or prevent.'" (Drown v. United States, supra, 198 F.2d 999, 1006, quoting United States v. Kordel, supra, 164 F.2d 913, 916.)

These events then make clear that laetrile poses two strong risks to the health of the population. Not only is laetrile itself hazardous but also by delaying conventional therapy it allows the cancer to proceed without any type of effective countermeasures. This two edged danger illustrates the terrible potential harm in allowing the "terminal cancer patient"<sup>4</sup> to have access to the drug. By allowing such access, that action communicates to other treatable cancer patients that there may be some value in laetrile. This would only serve to encourage them to abandon those forms of therapy already proven safe and effective and pursue unproven and unsafe alternate means. Thus, there is a tremendous potential harm to the population, by even allowing such so called terminal patients access to laetrile.

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4. This of course assumes that it would somehow be possible to formulate adequate definitional terms to identify this group. As the FDA Commissioner's decision makes clear, such a classification scheme is probably impossible. (42 Fed.Reg. 39805 (Aug. 5, 1977).)

These recent events thus only serve to further support the original findings of FDA Commissioner Kennedy that laetrile was neither safe or efficacious. Moreover, there is conclusive evidence of the toxicity of laetrile. Given this potential for harm, the necessity for premarket approval is clearly the obligation of a government concerned with the welfare of its citizens.

#### CONCLUSION

For the reasons submitted above, amicus curiae, the State of California, respectfully submits that the premarket demonstrations of safety and efficacy as required by 21 U.S.C. § 355 is not only constitutionally proper but also realistically needed for the protection of the welfare of the citizens of the United States.

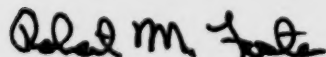
Respectfully submitted,

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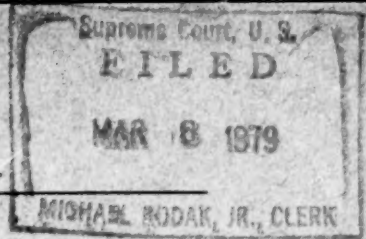
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**In the  
Supreme Court of the United States.**

OCTOBER TERM, 1978.

No. 78-605.

UNITED STATES OF AMERICA, ET AL.,  
PETITIONERS,

v.

GLEN L. RUTHERFORD, ET AL.,  
RESPONDENTS.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF  
APPEALS FOR THE TENTH CIRCUIT.

**Brief Amicus Curiae of the Commonwealth of Massachusetts  
and the Massachusetts Department of Public Welfare.**

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**Brief Amicus Curiae of the Commonwealth of Massachusetts  
and the Massachusetts Department of Public Welfare.**

### Interest of the Amicus.

Pursuant to Supreme Court Rule 42(4), the Commonwealth of Massachusetts and its Department of Public Welfare, sponsored by the Attorney General of the Commonwealth, submit this amicus curiae brief to support the position of the United States of America that the safety and effectiveness requirements of the Federal Food, Drug and Cosmetic Act apply to drugs intended for use by the terminally ill.



Like most states,<sup>1</sup> the Commonwealth has enacted legislation which effectively prohibits the in-state sale, distribution or use of any new drug not approved by the Food and Drug Administration (F.D.A.). M.G.L. c. 94C. To the extent that this Court finds the F.D.A.'s restrictions on the use of laetrile by the terminally ill to be constitutionally infirm, the analogous provisions of Massachusetts law are also threatened. Therefore, Massachusetts has a direct interest in protecting its citizens, including the terminally ill, from ineffective and potentially dangerous drugs, and therefore has a direct interest in the outcome of this case.

Massachusetts has also had recent experiences relating specifically to the controversy over laetrile — experiences which would appear to conflict with the assumption made by the Court below that laetrile is non-toxic. The Attorney General represents the Department of Public Welfare in the Chad Green matter in which the parents currently propose to add “metabolic therapy” to court-ordered chemotherapy. *Custody of a Minor*, \_\_\_ Mass. \_\_\_, 379 N.E. 2d 1053 (1978); *Green v. Truman*, 459 F. Supp. 342 (D. Mass. 1978); *Custody of a Minor*, No. 78-6816 (Plymouth, Mass., Superior Court, 1979).

Involvement in this case has given the amicus insights into the laetrile controversy and specifically into the toxicity of the substance which bear directly upon the matters before the Court in the instant case. Therefore, this brief is filed to assist the Court in consideration of the ramifications of the instant case on laetrile-related matters before the states.

<sup>1</sup> Schwartz, “Laetrile: The Battle Moves into the Courtroom,” 65 ABAJ 224 (1979).

## Questions Presented.

Whether the safety and effectiveness requirements of the Federal Food, Drug and Cosmetic Act apply to drugs intended for use by the terminally ill.

## Statement of the Case.

The Commonwealth of Massachusetts adopts and incorporates herein the statement of the case set forth in the Petitioner's brief.

## Argument.

### Reasons for Deciding in Favor of the United States.

#### I. THE MEDICAL AFFIDAVIT SYSTEM CREATED BY THE COURT OF APPEALS IS UNWORKABLE.

The Court of Appeals in *Rutherford v. United States*, 582 F. 2d 1234, 1237 (10th Cir. 1978) (*Rutherford VI*), determined that the “safety” and “effectiveness” prerequisites which must be established for new drug approval (21 U.S.C. § 355(d)) do not apply to terminally ill patients.

We conclude, however, that the permanent injunction granted by the district court should be continued but be limited only to permit procurement of *intravenous injections* administered by a licensed medical practitioner to persons who are *certified by a licensed medical practitioner to be terminally ill of cancer* in some form. *Rutherford VI*, *supra* at 1237 (emphasis added).

The Tenth Circuit assumed "that no applicable or reasonable measure exists" to determine a drug's safety and effectiveness for a terminally-ill patient. *Ibid.* This is an incorrect assumption. A drug's safety and effectiveness for any patient can be determined with regard to a drug's ability to reduce pain, or to counteract symptoms of disease. Nevertheless, assuming *arguendo* that no such measure of effectiveness does exist, then the efficacy of the certification process becomes the primary focus. The immediate question concerns the present ability of medical science to distinguish between a terminal and non-terminal cancer patient. Several expert submissions included in Food and Drug Administration, "Laetrile: Commissioner's Decision on Status," 42 *Fed. Reg.* 39,767 (August 5, 1977), cast severe doubt on the present ability of medical knowledge to make such a distinction. For example,

Dr. Peter H. Wiernik, Chief of the Clinical Oncology Branch of the National Cancer Research Center, states, "one major difficulty in making a particular chemical available for terminal patients only is that *no one can prospectively define the term 'terminal' with any accuracy.* A patient can be said to be terminal only after he dies. Many patients who are critically ill respond to modern-day management of cancer." (Emphasis added.) Food and Drug Administration, *supra* at 39,805 (August 5, 1977).

Several other cancer researchers echoed Dr. Wiernik's statement.<sup>2</sup>

<sup>2</sup> Note, "Laetrile: Statutory and Constitutional Limitations on the Regulation of Ineffective Drugs," 127 *U. Pa. L. Rev.* 233, 254-255 (1978) (author aptly notes that definitional problem is inherent in nature of cancer, which varies greatly in behavior, rate of growth, symptoms, amount of bodily intrusion, and chances of recovery for patient).

A corollary to this definitional problem is the high probability of intentional abuse of the certification system proposed by the Court of Appeals. In *Custody of a Minor*, No. 78-6816 (Plymouth, Mass. Superior Court, 1979), the child suffers from acute lymphocytic leukemia. His disease is not terminal. See George, Aur, Mauer and Simone, "A Reappraisal of the Results of Stopping Therapy in Childhood Leukemia," 300 *N. Eng. J. Med.* 269 (1979). Nonetheless, one of the parent's medical experts testified that he would certify the child under *Rutherford VI* as a terminal cancer patient in order to give him laetrile. This was true even though (1) the child is not terminally ill and (2) the child is receiving laetrile tablets rather than injections. See also *Custody of a Minor*, \_\_\_ Mass. \_\_\_, 379 N.E. 2d 1053 (1978). It would appear that the prospective conduct of that expert is not aberrational. For example, newspaper reports concerning a Mrs. Pye, who died of acute cyanide poisoning after an accidental overdose of laetrile, reveal that she had a *Rutherford VI* affidavit, even though she was taking laetrile tablets. *The Boston Globe*, February 7, 1979, at 62, Col. 1. Thus, the affidavit system permitted by the court in *Rutherford* is simply unworkable. Given the toxic effects of laetrile and metabolic therapy discussed below, on the one hand, and the problem of definition and intentional abuse on the other, the decision of the Tenth Circuit should be reversed.

## II. THE GOVERNMENT HAS A COMPELLING INTEREST IN PROTECTING THE PUBLIC FROM DANGEROUS DRUGS.

This case demonstrates the interaction between the constitutional right to privacy and the duty of government to protect the public from dangerous drugs. The District Court based

its decision on the constitutional right to privacy. The Court of Appeals did not deal directly with this issue:

We do not reach the constitutional aspects which were applied by the district court. We conclude, however, that the permanent injunction granted by the district court should be continued but be limited only to permit procurement of *intravenous injections* administered by a *licensed medical practitioner* to persons who are certified by a licensed medical practitioner to be terminally ill of cancer in some form. *Rutherford VI, supra*, at 1237 (emphasis added).

The District Court in *Rutherford v. United States*, 438 F. Supp. 1287, 1299 (W.D. Okla. 1977) (hereinafter *Rutherford V*), based its decision on the constitutional right of privacy articulated by this Court in such cases as *Roe v. Wade*, 410 U.S. 113 (1973), and *Doe v. Bolton*, 410 U.S. 179 (1973). In *Rutherford V*, the court, *supra* at 1300-1301, correctly identified the standard which must be met before there may be state interference with the constitutional right of privacy:

When certain "fundamental rights" are invoked, such as the right of privacy involved herein, regulation may be justified only by a "compelling state interest," and legislative enactments "must be narrowly drawn to express only the legitimate state interests at stake."

The District Court based its conclusion about the constitutional right of privacy on the mistaken assumption that laetrile is not toxic, stating that: "By denying the right to use a *nontoxic substance* in connection with one's own personal health-

care, FDA has offended the constitutional right of privacy." *Id.* at 1301 (emphasis added).

Amicus suggests, however, that laetrile is highly toxic and this alone constitutes a sufficiently compelling state interest for prohibiting selective laetrile use by the terminally ill or anyone else. It is well-accepted that the FDA has a responsibility to protect the public from dangerous drugs being available on the market.

"There can be no question of the authority of the State in the exercise of its police power to regulate the administration, sale, prescription and use of dangerous and habit-forming drugs . . . . The right to exercise this power is so manifest in the interest of the public health and welfare, that it is unnecessary to enter upon a discussion of it beyond saying that it is too firmly established to be successfully called in question." *Robinson v. California*, 370 U.S. 660, 664 (1962), quoting from *Whipple v. Martinson*, 256 U.S. 41, 45 (1921).

See also *Whalen v. Roe*, 429 U.S. 589, 603, fn. 30 (1977).

The Food, Drug and Cosmetic Act, 21 U.S.C. § 355(a)<sup>3</sup> and (d)(2),<sup>4</sup> provides the necessary authority to keep such "unsafe" drugs off the market. Therefore, if the toxicity of laetrile can be established, the necessary compelling state interest for

<sup>3</sup>"(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug. . . ."

<sup>4</sup>"(d) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section . . . , that . . . (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions . . . he shall issue an order refusing to approve the application. . . ."



allowing the FDA to ban laetrile will have been demonstrated. The right of privacy must give way before this compelling state interest.

The evidence currently available demonstrates that laetrile (or more accurately its generic term, amygdalin) contains toxicologically significant amounts of cyanide. *Dorland's Illustrated Medical Dictionary* (24th Ed. 1965) at 73 (definition of amygdalin). In National Academy of Sciences, *Toxicants Occurring Naturally in Foods* (2d Ed. 1973) at 449-450, the toxicity of amygdalin is clearly demonstrated:

Hydrogen cyanide (HCN) is released by enzymatic hydrolysis of a number of glycosides found in food. Oil of bitter almonds, a generic name for pit oils, including also oils of apricot and peach kernels, contains the glycoside amygdalin. The enzyme emulsin is also present, and when the pits are crushed and moistened, the glycoside is cleaved with the liberation of hydrogen cyanide. . . .

*Toxicologically significant dietary intakes of cyanide result either from improper choice of plant variety, as with some lima beans, inadequate processing, as may occur with cassava, or accidental intake, as in the case of a 3-year-old girl who incurred cyanide poisoning from eating approximately 15 apricot kernels containing 0.33% available CN. (Emphasis added.)*

Amygdalin (laetrile) is a cyanogenetic glycoside (cyanide-containing plant) which will yield the deadly poison hydrogen cyanide when the cyanide is cleaved out of the amygdalin. The circumstances when that will happen are as follows:

Bitter apricot kernels are little "cyanide pellets" because of their millions of subcellular organelles containing amygdalin and millions of other organelles (lysosomes) containing amygdalin and millions of other

organelles (lysosomes) containing B-glucosidase. The cyanide is "safe" as long as the apricot kernel is uncrushed, because it is tightly bound to the benzaldehyde of amygdalin. When an apricot kernel is crushed (by a blender, or the teeth, or anything else) the amygdalin and B-glucosidase make contact and cyanide is generated. The amount of cyanide generated is directly proportional to thoroughness of chewing the kernel. The process of cyanide release from an apricot kernel is analogous to dropping a sodium or potassium cyanide pellet . . . into water or acid, the means of "gas chamber" executions in California and genocidal mass killings by the Hitler regime during World War II. Herbert, "Laetrile: The Cult of Cyanide," 32 *Am. J. Clin. Nut.* (May, 1979) (in press). See also *Toxicants Occurring Naturally in Foods*, *supra* at 299-306.

A recent laetrile study with dogs confirms this conclusion,<sup>5</sup> and one commentator has noted that ingestion of laetrile itself has led to fatal acute cyanide poisoning:

A healthy 11-month-old girl accidentally swallowed one to five 500-mg. Laetrile tablets. The pills were labelled "kemdalin — each tab = 500 mgm amigdalin MF,

<sup>5</sup>"The literature contains numerous examples of human poisoning from eating apricot pits . . . since these tissues contain both amygdalin and the enzymes described. However, other plants, e.g., celery, peaches, and bean sprouts, contain B-glucosidases similar to those in almonds . . .

"Our studies were designed to confirm our prediction that oral laetrile, when ingested with certain uncooked foods containing B-glucosidases, would result in HCN toxicity. In our studies, we were able to reproduce the physiologic and clinical picture of HCN poisoning in dogs after the administration of laetrile and sweet almonds." Schmidt, et al., "Laetrile Toxicity Studies in Dogs," 239 *JAMA* 943 (1978). See *United States v. Articles of Food and Drug*, 444 F. Supp. 266 (E.D. Wis. 1977), *aff'd sub nom. United States v. Mostinee Research Corp.*, 583 F. 2d 930 (7th Cir. 1978).

. . . (LAETRILE)." The drug belonged to the patient's father, who was using it for the treatment of a cancer and considered the pills to be harmless vitamins . . .

In view of the hospital course and autopsy findings consistent with cyanide poisoning by the oral route, the cyanide demonstrated in blood and urine, and the negative studies for other possible toxins, we conclude that our patient died of subacute cyanide poisoning secondary to the accidental ingestion of amygdalin tablets. Braico, et al., "Laetrile Intoxication; Report of a Fatal Case," 300 *N. Eng. J. Med.* 238, 240 (1979).

See also, *The Boston Globe*, February 7, 1979, at 62, Col. 1 (article reporting December 3, 1978, death of 42-year-old California woman as a result of overdose of laetrile tablets).

Laetrile proponents admit that laetrile by itself is worthless but argue that laetrile must be used in conjunction with so-called metabolic therapy. Manner, *The Death of Cancer* (1978); Halstead, *Amygdalin (Laetrile) Therapy* (1977). However, the principal components of so-called "metabolic" therapy are themselves toxic in the dosages prescribed. They include a daily enema composed of proteolytic enzymes. These may destroy tissue in the colon. Goodman, L., and Gilman, A., *The Pharmacological Basis of Therapeutics* (5th Ed. 1975) at 958. Another component consists of megadoses of Vitamin A far above the recommended daily allowances. Vitamin A is fat soluble and will build up in the liver and cause hypervitaminosis A. See Goodman and Gilman, *supra* at 1574, and National Academy of Sciences, *Recommended Daily Allowances* (8th Ed. 1974) at 152. Another component is megadoses of Vitamin C which may affect fetal development. Herbert, "The Rationale of Massive-Dose Vitamin Therapy (Mega Vitamins Therapy: Hot Fictions vs. Cold Facts)," in P. White and N. Selvey, *IV Proceedings: Western Hemisphere Nutrition*

*Congress* 84, 87 (1975). It is indisputable that cyanide toxicity can cause acute poisoning leading to death (as at Jonestown). Smaller intakes of cyanide lead to chronic cyanide poisoning. In *Custody of a Minor*, No. 78-6816 (Plymouth, Mass., Superior Court, 1979), the child was shown to be suffering from chronic cyanide poisoning as a direct result of his daily intake of one 500-mg. laetrile tablet. There was expert testimony that the child had a cyanide level in his blood which was comparable to that of a heavy adult smoker. That this level of cyanide will culminate in progressive deafness and blindness by poisoning from laetrile is well-documented in the literature.

Chronic cyanide intoxication from laetrile in the diet has produced in Africa thousands of cases of slowly progressing neurologic damage with blindness (bilateral optic atrophy), nerve deafness, and myelopathy, with muscle weakness in a demyelinating syndrome of toxic ataxic neuropathy and variants of it. Herbert, "Laetrile: The Cult of Cyanide," *supra*; see also *Toxicants Occurring Naturally in Foods, supra* at 305; B.O. Osuntokun, "Cassava diet and cyanide metabolism in Wistar rats," 24 *Br. J. Nutr.* 797 (1970); "Chronic Cyanide Neurotoxicity," ii *Lancet* 942 (1969). See generally United States Senate, Subcommittee on Health and Scientific Research, Committee on Human Resources, 95th Cong., 1st Sess., *Banning of the Drug Laetrile from Interstate Commerce by FDA* (Comm. Print 1977).

### III. THE CONSTITUTIONAL RIGHT OF PRIVACY MUST GIVE WAY BEFORE THE COMPELLING NEED TO PROTECT THE PUBLIC FROM LAETRILE TOXICITY.

The constitutional right of privacy applies to the relationship of physician and patient. *Loe v. Bolton*, 410 U.S. 179

(1973). *But see Fitzgerald v. Porter Memorial Hospital*, 523 F. 2d 716 (7th Cir. 1975), *cert. den.* 425 U.S. 916 (1976). However, at the same time, "the State has broad police powers in regulating the administration of drugs by the health professions." *Whalen v. Roe*, 429 U.S. 589, 603, fn. 30 (1977). *See also Carey v. Population Services International*, 431 U.S. 678 (1977), and *Smith v. Organization of Foster Families for Equality & Reform*, 431 U.S. 816 (1977).

In regard to laetrile, some courts have found the privacy interest to be paramount. For example, a California intermediate appellate court has held that:

This state protected right of privacy encompasses a fundamental and compelling interest of the cancer patient to choose or reject his or her own medical treatment on the advice of a licensed medical doctor. This right can be abridged only where there is compelling need. *People v. Privitera*, 74 Cal. App. 3d 936, 141 Cal. Rptr. 764, 777 (1977). (The case is awaiting decision by the California Supreme Court and thus the decision of the intermediate appellate court has no precedential value.)

The *Privitera* court found that the state had not established the compelling need necessary to abridge the right of privacy.

However, "The Legislature has the right to control distribution and use of drugs which are narcotic, habit forming, hallucinatory or toxic . . . but to limit its power to just these kinds of drugs portends a frightening parade of horrors. Protection of public health, safety and welfare demands more." *People v. Privitera*, *supra*, 141 Cal. Rptr. at 787 (Cologne, J., dissenting). The purpose of the Food, Drug and Cosmetic Act and of similar state statutes is to protect the public from unproven, unsafe or ineffective drugs. 21 U.S.C. § 351; *United*

*States v. Bel-Mar Laboratories, Inc.*, 284 F. Supp. 875 (E.D. N.Y. 1968). Laetrile has been shown to be toxic because of the presence of cyanide. *See* Sadoff, Fuchs and Hollander, "Rapid Death Associated with Laetrile Ingestion," 239 JAMA 1532 (1978); and Townsend and Boni, "Cyanide Poisoning From Ingestion of Apricot Kernels," 24 *Morbid Mortal* 427 (1975). "Amygdalin [laetrile] is not generally recognized by experts qualified by scientific training and experience to evaluate its safety, as having been shown through scientific procedures . . . to be safe under the conditions of its use." *United States v. General Research Laboratories*, 397 F. Supp. 197, 199 (C.D. Cal. 1975). The District Court in *United States v. Articles of Food and Drug*, *supra*, found that,

1. "Amygdalin is a cyanogenic glucoside [*sic*] which reacts with Beta-glucosidase, an enzyme found in a number of commonly eaten foods, to form hydrogen cyanide, a highly toxic substance." *Id.* at 271.

2. "Due to the presence therein of cyanide, a poisonous and deleterious substance, amygdalin is potentially harmful and ordinarily injurious to health." *Ibid.*

3. "The promotion or sale of amygdalin for any food or drug use constitutes a fraud on the consuming public." *Id.* at 273.\*

Therefore, the FDA should be upheld in its efforts to eliminate laetrile from the marketplace.

\*There is less indication of toxicity of injected laetrile since the cyanide is not liberated by Beta-glucosidase and probably passes through the body whole. Herbert, "Laetrile: The Cult of Cyanide," *supra*, at \_\_\_\_ (in press); on the other hand, there is no reliable evidence that injected laetrile has anti-neoplastic capabilities. Stock, et al., "Antitumor Tests of Amygdalin in Spontaneous Animal Tumors," 10 *J. Oncology* 89 (1978).



Finally, there is a second aspect to the compelling interest argument. The carving out of an exception to the Food, Drug and Cosmetic Act for the terminal patient may either lead a non-terminal patient to forgo effective treatment or cause a patient currently undergoing effective treatment to shift to unproven treatments. See *Custody of a Minor, supra*; *In re Hofbauer*, 411 N.Y.S. 2d 416 (App. Div. 1978). These problems are very real because of the relative ease with which any patient can acquire a "Rutherford affidavit." The results can only be needless suffering for those persons who mistakenly decline beneficial treatment because of the lure of unsafe remedies.

#### Conclusion.

For the reasons articulated in the argument, the decision of the Court of Appeals should be reversed.

Respectfully submitted,

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MAR 8 1979

MICHAEL J. BODAN, JR., CLERK

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IN THE  
**Supreme Court of the United States**  
OCTOBER TERM, 1978

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No. 78-605

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UNITED STATES OF AMERICA, *et al.*,  
*Petitioners*

v.

GLEN L. RUTHERFORD, *et al.*,  
*Respondents*

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On Writ of Certiorari to the United States  
Court of Appeals for the Tenth Circuit

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BRIEF AMICUS CURIAE OF THE  
AMERICAN CANCER SOCIETY, INC. IN SUPPORT OF  
PETITIONER, THE UNITED STATES

---

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On Writ of Certiorari to the United States  
Court of Appeals for the Tenth Circuit

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BRIEF AMICUS CURIAE OF THE  
AMERICAN CANCER SOCIETY, INC. IN SUPPORT OF  
PETITIONER, THE UNITED STATES

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STATEMENT OF INTEREST OF  
THE AMERICAN CANCER SOCIETY

The American Cancer Society has a substantial interest in the outcome of this proceeding. Briefly stated, the American public and the medical profession look to the American Cancer Society to provide the most up-to-date and accurate information about cancer. Since early and effective treatment of cancer is a life and death

matter, one of the areas in the forefront of the public and professional questioning addressed to the Society pertains to unproven methods of cancer treatment. In its efforts to respond to the need for information in this area, the Society established a committee on unproven methods and maintains one of the largest reference centers for the collection and dissemination of data concerning the subject. In furtherance of its obligation to the American public and the medical profession to uncover and disseminate the facts relating to unproven methods of cancer treatment, the Society participated in the Food and Drug Administration rulemaking proceeding which followed the legal parameters set by the Court of Appeals in *Rutherford v. United States*, 542 F.2d 1137, 1140-43 (10th Cir. 1974). (Petitioners' Appendix at 51d). The Society also participated as amicus curiae in the proceedings on appeal which are the subject of this petition. (Petitioners' Appendix at 10a).

The outcome of the Government's appeal which the Society supports will be largely determinative of whether the protections provided by Congress to the American public in the Food Drug and Cosmetic Act will survive or whether they will fall, depriving both the consumer and the practicing physician of the first line of defense established by Congress at the request of President Kennedy who stated:

There is no way of measuring the needless suffering, the money innocently squandered, and the protraction of illnesses resulting from the use of . . . ineffective drugs.

The physician and consumer should have the assurance from an impartial scientific source, that any drug or therapeutic device on the market today is safe and effective for its intended use . . . .

1962 U.S. Code Cong. & Admins. News at 4143-44. Either the impact of the *Rutherford* Court of Appeals decision,

which writes off the safety/efficacy provisions of the federal drug laws as they apply to the terminally ill, or the impact of the alternative grounds for decision of the district court, which finds both a grandfather clause exemption for Laetrile and a right of privacy in its use, will obviously affect the Society in its role as primary information source to the general public and the medical profession for accurate information on unproven methods of cancer treatment.

Should the *Rutherford* decision stand, another indication of its impact on the public, and the Society as its information resource lies in the resurgence, since mid-1976 when the *Rutherford* suit became heavily publicized, of inquiries about a number of unproven methods of cancer treatment in addition to laetrile. Prior to the *Rutherford* publicity, some of these methods were quiescent for months or years or came to the Society's attention at long scattered intervals. Those unproven methods include, e.g., the biological theory of ionization; wobe mugs; herbal remedies such as one called essiac; chelation therapy and alleged vaccines combined with special diets.

By way of specific illustration, a complaint for forfeiture is pending before a district court in California<sup>1</sup> involving:

"Wobe Mugs products in the treatment of Cancer, Herpes Zoster and Herpes simplex; and

Wobenzym preparations in the treatment of cancer, arteriosclerosis, angina, asthma, arthritis, bursitis, circulatory disorders including diabetic circulatory disease, intermittent claudication, phlebitis and thrombophlebitis, varicose ulcers, pneumonia, cysti-

<sup>1</sup> United States v. Articles of Drug consisting of . . . WOBÉ MUGOS Lozenges, No. CV 78-3736 AAH(KY) (United States District Court, Central District of California) (September 28, 1978).



tis, emphysema, and gynecological and urological inflammatory disorders."

If the Court of Appeals' decision is permitted to stand, it will open the floodgates and permit the public, particularly those with life-threatening illness who are choice prey, to be inundated by worthless and therefore unsafe and dangerous drugs. The Society's interest lies in speaking out for the continuation of the proper balance of manufacturer and consumer interests which currently exists in the statutory scheme relating to drugs. It would be a grave disservice to the public if this regulatory scheme were undermined on the basis of a Court of Appeals or on the alternative grounds advanced by the district court opinion which we demonstrate below is unsound as a matter of law.

The American Cancer Society has received the consent of counsel for all parties to file this brief *amicus curiae* in accordance with Rule 42 of this Court. Those permissions are attached to the original of this brief filed with the Supreme Court.

#### SUMMARY OF THE ARGUMENT

*The court of appeals exemption of the terminally ill from the pre-marketing requirements of the federal drug laws.* The plain language of the federal drug laws does not signal any exemption from coverage for the terminally ill. To the contrary, the legislative and administrative history of those laws and their interpretation by the courts show a specific intent to safeguard consumers with life-threatening and terminal illnesses. The holding of the court of appeals exempting the terminal from these pre-marketing clearance provisions runs against this intent and also contra to the decisions of other federal courts who, faced with drug law challenges by a patient class of the terminally ill, have held these laws applicable to that class. Further, although it is theo-

retically possible to formulate a definition of terminally ill, the objective application of that definition is improbable. The record in this proceeding shows abuses which will permit other than those certified as terminally ill to have access to laetrile and those abuses have also surfaced in other proceedings in federal and state courts. Finally, the public interest requires application of the premarketing clearance requirements of the federal drug laws for the benefit of all consumers including the terminal. When the nebulous benefits of access to a drug generally recognized to be ineffective and unsafe to the in-fact terminally ill, those with only a few weeks or months to live, against the very real threat of exemption and broadening of access to those whose cancer is in the early stages, treatable and merely life-threatening.

*The district court's application of the 1962 grandfather clause.* The district court improperly shifted the burden of proceeding and proof in the rulemaking proceeding from the drug proponents on whom it properly rests to the Food and Drug Administration. However, even under the improperly shifted burdens of proof, the record establishes the error of the district court exempting Laetrile from the premarketing requirements of the federal drug laws by application of the 1962 grandfather clause. Laetrile does not satisfy the grandfather clause requirements of (1) consistency and predictability in drug formulation, dosage, route of administration, mechanism of action, claims and conditions for usage and effect; (2) its use prior to 1962 was investigational and not commercial; and (3) it is not generally recognized by qualified experts in cancer treatment as safe or effective. Where life-threatening illness is involved the administration interpretation of "safety" under the 1938 Act period included toxicity and effectiveness. This administrative interpretation was adopted by Congress when it considered the 1962 Drug Amendments and thus Laetrile must be generally recognized as effective as well as

safe (non-toxic) before it can receive the exemption contemplated by the 1962 grandfather clause.

*The district court's holding that laetrile use in personal health care is protected by the Constitution.* An analysis of this Court's decisions regarding "privacy" in the context in which they were rendered shows that the selection of a particular drug or medical treatment procedure is not invested with privacy status. The decision whether to receive medical treatment may be constitutionally protected but the choice among treatment alternatives is not within the scope of any right recognized by this Court. Further, if a privacy right is found by this Court, the nexus of the premarketing provisions of the federal drug laws with the preservation and protection of the health of the cancer patient justifies government regulation under both the rational relationship and compelling interest tests.

#### ARGUMENT

#### I. THE COURT OF APPEALS REVISION OF THE FEDERAL DRUG LAWS TO EXEMPT THE TERMINALLY ILL NOT ONLY FLIES IN THE FACE OF CONGRESSIONAL INTENT BUT ALSO EFFECTIVELY DEPRIVES THOSE WITH LIFE-THREATENING ILLNESS OF THE PROTECTIONS OF THE ACT

##### A. Overview of the Problem

The Court of Appeals did not address the issues of whether Laetrile was generally recognized as safe and effective among qualified experts, nor whether it is grandfathered, nor did it address the additional ground of decision advanced by the district court—the alleged Constitutional right to privacy. Rather, the court of appeals held "as a matter of law that the 'safety' and 'effectiveness' requirements of the statute as now written have no application to terminally ill cancer patients who

desire to take the drug [Laetrile] intravenously." (Petitioner's Appendix 7a, hereinafter stated as "Pet. App.>"). This holding has a surface appeal. If a person is going to die, why not indulge him by permitting access to any alleged cancer remedy he may wish to try. The reasons for denial of such permission are many.

The court of appeals assumes that an objective standard is available or can be formulated and applied to determine who is "terminally ill." This assumption is in conflict with the findings made by the Commissioner in the Laetrile decision, (Pet. App. at 267a-270a). The thrust of those findings is that cancer is a disease that affects individual patients and that physicians dealing with these patients on an individual basis find it difficult to distinguish the in-fact terminal from non-terminal cancer patients with any accuracy. The practical and ethical problems of carving out an exception for the terminally ill from the Act was pointedly addressed by Dr. Samuel Klagsbrun in his affidavit (Ad. R. 433).<sup>2</sup>

Use of the term "terminally ill" is inappropriate when dealing with an individual cancer patient. Although specific forms of cancer may have a statistically expectable mortality rate, that rate is meaningless when applied to an individual patient. Oncologists are all familiar with experiences where severe cancers, which were statistically considered to be hopeless, have, in some small percentages of cases, undergone a sudden remission. It would be tragic to condemn any individual cancer patient to

<sup>2</sup> The record transmitted to this Court made a distinction between the record compiled during the Laetrile rulemaking proceeding and the record specifically developed before the district court. This distinction will be observed in the Society's brief. References to the administrative record will be cited Ad.R. —; or administrative transcript, Ad.Tr. —; references to the court record will be cited Ct.R. —; or if a district court hearing transcript is involved Ct.Tr. —.

death because, as a statistical matter, that patient's particular form of cancer may not be curable.

A decision to allow patients who are diagnosed as having a cancer which, as a statistical matter expected to lead to their death, would move all such patients away from orthodox therapy and condemn even the individual patient whose cancer may unexpectedly move into remission to Laetrile, a worthless and ineffective drug. In addition, such a decision would thereafter remove the patients from the possibility of receiving continuing chemotherapy or radiation therapy which could enhance the effects of any remission. Most physicians have undergone the experience of predicting the moment of death and have unexpectedly and repeatedly been proven wrong to a considerable degree. The prolongation of life, therefore, becomes a goal, not simply for the sake of prolongation, but also to render patients available to either a recent advance in chemotherapy or simply to enhance the quality of the time left available to the patients.

Even if we assume theoretically that the phrase "terminally ill" may be capable of objective application,<sup>3</sup> in practice, in the district court proceeding, tight objective standard criteria court proceeding, tight objective stand-

<sup>3</sup> Robert S.K. Young, M.D. (Ct.R. 210-211) indicated before the district court what he considered to be the criteria for determining whether a patient is terminal:

"a. There must be histologic evidence of a malignancy in the patient.

b. The malignancy must be characterized as a disease with a high and predictable mortality. It must also be rapidly progressive. The malignancy will result in death in a relatively short period of time, i.e., within a few weeks or within a few months."

c. There must be no treatment recognized by experts as safe and effective for the disease, or therapies recognized as safe and effective for the disease have been totally exhausted, and further treatment would not be reasonably expected to benefit the patient.

ard criteria has been eschewed.<sup>4</sup> Instead, the district court proceeding employed an affidavit process that does not present a reasonable certainty that laetrile access will be confined to those who are in fact terminally ill.<sup>5</sup>

Further, the record in the district court, discussed in Section D hereto shows the abuse of the affidavit process to permit importation of laetrile far in excess of patient requirements to be disposed of to cancer patients who have not been certified terminally ill by affidavit.

<sup>4</sup> The FDA in its policy of the implementation of the affidavit process for access to laetrile put into effect by the district court to assume that the legitimately terminal alone were permitted access to laetrile, also required the patients affidavit subjects to possess a doctors affidavit that they will probably die within a few weeks or a few months and also to show proof that they had a medical exam within the last three months (Ct.R. 309-310). The Government contended that this would be the only way to assure that the patients receiving laetrile were in fact terminal (Ct.R. 315-316).

The rationale behind this information requirement was explained by Dr. Young at Ct.R. 331-334:

"The essential first step in making an accurate medical diagnosis of a malignancy, as opposed to mere speculation as to a patient's condition, is the obtaining of histologic evidence and characterization of the disease. This information compiled with a thorough physical examination and appropriate diagnostic laboratory tests including radiologic and scintillation studies and intimate knowledge of the natural history of the disease enables a physician realistically and reasonably to reach a conclusion as to whether a particular tumor can be characterized as one which is usually rapidly progressive and which, if untreated, normally results in a high and predictable mortality rate."

<sup>5</sup> The district court's reaction to this rationale was to add a condition that the date of examination be noted on the affidavit form (Ct.R. 337-338). Further, since the affidavit does not require a physician to refuse to execute the affidavit if orthodox modalities are not also employed or if other orthodox therapies of benefit are available but can justify execution on presence of progressive cancer plus informed consent, there is no assurance that only those without medical alternatives will legally import laetrile. See e.g., Ct.R. 481-484, 490, 493, 496, 499, 502.



In addition, a laetrile proceeding involving a minor, shows that the term "cancer" has been incorrectly treated as synonymous with "terminal" to obtain access to the drug. In the proceeding involving a minor, a physician has stated that even if he did not believe a patient terminal, he would so certify to assure the patient's access to laetrile.

These aspects of exemption and the effect of exemption on the larger class of cancer patients whose disease is merely life-threatening are discussed in detail in Section D at pp. 23-33 *infra*. However, the most significant obstacle to the exemption created by the court of appeals springs from its absolute inconsistency with the intent of Congress as expressed initially in the Pure Food and Drug Act of 1906 and culminating in the 1962 Drug Amendments, discussed immediately below.

**B. From the Exercise of Federal Authority Over Drugs Initially By The Act of 1906, And As Amended, The Terminally Ill Lay Within The Special Protection Of The Acts**

The medical and popular press in the early 1900's reflected the sense of the country at that time that the words cancer and terminal illness were interchangeable. E. Cuyler Hammond, D.Sc., Director of Statistical Research Section of the American Cancer Society, writing in *Cancer* 417 (Butterworth & Co., London, 1958) described the public's impression of cancer in the first quarter of this century as "incurable" and further stated that this conception was shared by a large proportion of the medical profession. This impression was certainly borne out by the literature which reported the survival rate for, e.g., uterine cancer in 1900, to be as low as 2.8%.<sup>6</sup>

<sup>6</sup> T.S. Cullen, *Cancer of the Uterus* (1900). See also, E.C. Hammond, "Cancer Prevention of Comparative Risks", 19 *Archives of Environmental Health* 395 (1969); and see J.S. Bloodgood, "Responsibility of the Medical Profession for Cancer Education, with

These statistics improved somewhat. Indeed, between 1935-1940, the five year survival rate for all sites of cancer combined reached 25%, by 1951 it reached 32%.<sup>7</sup> However, even in 1967, public and physician reaction to the term cancer still equated it with a death sentence:

Cancer has many unconscious meanings and fantasies associated with it. Whatever the unconscious feelings which it stirs, typically it is feared consciously as a process equated with suffering and certain death . . . People continue to think of cancer as 'the killer.'

What is impressive is that the doctors themselves feel very much the same way. It was not patients who described the diagnosis as a 'death warrant' or 'a date of execution.' The internist who referred to cancer as an 'incurable disease with an inevitable demise' expressed a view which was not atypical.<sup>8</sup>

As late as the summer of 1977, in Hearings before Senator Edward Kennedy's Subcommittee on Health and Scientific Research,<sup>9</sup> Lewis Thomas, M.D., Director of the Memorial Sloan-Kettering Cancer Center, observed that "For many patients and their families, the very word cancer is perceived as a death sentence. It is widely

Special Reference to Cancer of the Cervix", 15 *American Journal of Cancer* 1579 (1931) (cancer of the cervix is today predominantly a hopeless disease).

<sup>7</sup> E.C. Hammond, "The Possibility of Improving Cancer Cure Rates at the Present Time", *Cancer*, May-June 1957 at 581-582; *Proceedings of the Third National Cancer Conference* 910 (1957).

<sup>8</sup> Donald Oken, "What to Tell Cancer Patients: A Study of Medical Attitudes", reprinted in Weir, *Ethical Issues in Death and Dying* (1977) at 21.

<sup>9</sup> Hearings Before the Subcommittee on Health and Scientific Research of the Senate Committee on Human Resources, "Evaluation of Information on Which the FDA Based Its Decision To Ban The Drug Laetrile From Interstate Commerce", 95th Cong., 1st Sess (1977) ["Laetrile Hearings"].

believed to be an inexorable and agonizing process, with no way out but death.”<sup>10</sup>

The early concern of the public and the press that the “seriously” or “terminally” ill be protected from useless nostrums is perhaps best exemplified by a series of articles by Samuel Hopkins Adams—published in *Collier's Weekly* in 1906. These articles sought to enlighten the general public regarding the effects of various patent legislation regulation drugs.<sup>11</sup> A segment of the series contained the following passage, entitled, “Preying on the Incurables”:

Incurable disease is one of the strongholds of the patent-medicine business. The ideal patron, viewed in the light of profitable business, is the victim of some slow and wasting ailment in which recurrent hope inspires to repeated experiments with any “cure” that offers. In the columns of almost every newspaper you may find promises to cure consumption. Consumption is a disease absolutely incurable by any medicine . . . This is thoroughly and definitely understood by all medical and scientific men. Nevertheless there are in the patent-medicine world a set of harpies who, for their own business inter-

<sup>10</sup> Laetrile Hearings, *supra* at 13.

This popular belief contrasts strongly with the actual statistics relating to survival from cancer due to earlier diagnosis and the steady improvement in surgical, x-ray and chemical approaches to the management of cancer. In the 1900's few cancer patients had any hope of long-term survival. In the 1930's less than one-in-five were alive at least five years after treatment. In the 1950's it was one-in-four. Now the ratio of patients alive after five years of disease is one in three. With even earlier diagnosis and prompt treatment, half of those who have cancer could be saved. See American Cancer Society, 1977 Cancer Facts and Figures, and see the 5 year survival statistics for specific sites of cancer when early diagnosis is made *infra* at note 30 which shows survivals of up to 86% of selected sites.

<sup>11</sup> See Cramp, Nostrums & Quackery (1912) for a compilation of the Colliers articles and a discussion of their effect on the food and drug legislation of 1906.

ests deliberately foster in the mind of the unfortunate sufferer from tuberculosis the belief that he can be saved by the use of some absolutely fraudulent nostrum. Many of these consumption cures contain drugs which hasten the progress of the disease . . . Others are comparatively harmless in themselves, but by their fervent promises of rescue they delude the sufferer into misplacing his reliance and forfeiting his only chance by neglecting those rigidly careful habits of life which alone can conquer the “white plague.” One and all, the men who advertise medicines to cure consumption deliberately traffic in human life.<sup>12</sup>

The inclusion of several of the Colliers Articles in the Congressional Record<sup>13</sup> and also numerous citations in the Pure Food and Drug Act debates of reported frauds perpetrated upon the victims of such serious illness as cancer, consumption and diabetes in the form of spurious claims for cures,<sup>14</sup> indicates a significant concern with those illnesses which in 1906 were “terminal” and by inference a determination by Congress that the “terminally ill” as a class would be protected by the legislation.

In face of this concern over the application of the 1906 Act to cancer, consumption and other illness which were then considered fatal, the Congress expressed disbelief when the Supreme Court in *United States v. Johnson*, 221 U.S. 488 (1911), a case which concerned a purported treatment for cancer, over a strong dissent by Justice Hughes, held that the 1906 Act did not apply to misrepresentations of facts relating to the ability of a drug to treat or cure a disease, but rather, only as to whether the ingredients used in the drug were properly stated on the label.

<sup>12</sup> 48 Cong. Rec., part 12, Appendix at 625-630.

<sup>13</sup> *Id.*

<sup>14</sup> See e.g., 40 Cong. Rec. 1416, 9073

In prompt response, President Taft, on June 21, 1911, in a message to Congress, urged action to protect the seriously ill against statements of curative effect on drugs that are contrary to fact and that seduce the ill away from proven medical treatments:

An evil which menaces the general health of the people strikes at the life of the Nation. In my opinion, the sale of dangerously adulterated drugs, or the sale of drugs under knowing false claims as to their effect on disease, constitutes such an evil and warrants me in calling the matter to the attention of the Congress.

Fraudulent misrepresentations of the curative value of nostrumes not only operate to defraud purchasers but are a distinct menace to the public health. There are none so credulous as sufferers from disease. The need is urgent for legislation which will prevent the raising of false hopes of speedy cures of serious ailments by misstatements of facts as to worthless mixtures on which the sick will rely while their diseases progress unchecked.<sup>15</sup>

The Congress reacted to this call for action by passing the Sherley Amendment to the Act [Act of August 23, 1912, 37 Stat. 416, ch. 352] which provided that misstatements regarding curative or therapeutic effects of a drug or device fall within the ambit of the Act.

In commentary upon the Sherley Amendments to the Act in the 1913 Report of the Bureau of Chemistry, Bureau Chief Carl L. Alsberg notes the early successes of the Amendment in terms of the curative claims found on medicinal labels. According to Alsberg, "Claims that preparations are cures for such serious diseases as tu-

<sup>15</sup> 48 Cong. Rec. 11322 (1911). See also, *Belmont Laboratories v. FTC*, 103 F.2d 538 (3rd Cir. 1939).

berculosis or cancer do not appear on the labels as often as formerly."<sup>16</sup>

The statutes extended protection afforded to those who suffer from untreatable or incurable disease is apparent from the opinion of Justice Hughes applying the Sherley Act Amendment to the 1906 Act in *Seven Cases . . . Eckman's Alternative et al. v. United States*, 239 U.S. 510, 514 (1916). Justice Hughes speaking for the Court, specifically upheld the following libel as a matter subject to prosecution under the Act as amended:

[The label] conveys the impression to purchasers that said article or drugs will cure tuberculosis, or consumption, whereas, in truth and in fact, said articles of drugs would not cure tuberculosis, or consumption, *there being no medicinal substances known at present which can be relied upon for the effective treatment or cure of tuberculosis, or consumption.* (emphasis added).

The concern of Congress and the courts with the assurance that the federal drug laws protect those with terminal or life-threatening was closely followed in the administrative interpretation of the Act. The administrative interpretation<sup>17</sup> of the federal drug laws ex-

<sup>16</sup> Federal Food and Cosmetic Law, Administrative Reports, 1907-1949, CCH, Food Law Institute Series (1951).

<sup>17</sup> Hearings Before the Subcommittee on Antitrust & Monopoly, Senate Committee on the Judiciary, 87th Cong., 1st Sess. on the "Drug Industry Antitrust Act", Part 5 at 2588. (emphasis added)

In testimony before Congress, the FDA stressed that under its view of existing law, the safety of a non-toxic drug could be construed to include efficacy only where the disease involved is life-threatening. See S. Rep. No. 1744 (part 1) 87th Cong., 2d Sess. 15; H. Rep. No. 2464, 87th Cong., 2d Sess. 3. And see Hearings on Drug Safety Before a Subcommittee of the H. Comm. on Government Operations, 88th Cong., 2d Sess., pt. 1, 150, 183-186 (Commissioner Larrick) and Hearings on Drug Efficacy Before A Subcommittee of the H. Committee on Government Operations, 91st Cong., 1st Sess. 228 (Commissioner Ley).

To the same effect see Federal Food, Drug and Cosmetic Law Administrative Reports 1907-1949 at 927.



tend special protection to those with life-threatening or terminal illnesses. The FDA construed the language in the 1938 Drug Act, which required new drugs to show "safety", also includes "efficacy":

It is important to recognize that evaluating effectiveness is not a new concept in the administration of the food and drug law. In some instances the decision as to safety of a new drug necessarily requires an evaluation of effectiveness. If the drug is offered for treatment of progressive or life threatening diseases, such as cancer, or if the drug is seriously toxic or has alarming side effects we now consider its effectiveness. In such cases the determination of safety is in the light of the purpose of the new drug provisions, inseparable from consideration of the drug's effectiveness."<sup>18</sup>

This prior administrative practice and its special, protective coverage for those with life threatening or progressive (terminal) disease was expressly recognized, endorsed and continued by Congress in the 1962 Drug Amendments.

The Food and Drug Administration now requires, in determining whether a "new drug" is safe, a showing as to the drug's effectiveness where the drug is offered for use in the treatment of a life-threatening disease, or where it appears that the "new drug" will occasionally produce serious toxic or even lethal effects so that only its usefulness would justify the risks involved in its use. In such cases, the determination of safety is, in the light of the purposes of the new drug provisions, consid-

<sup>18</sup> Id. at 2588. See *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609 (1973). With respect to the concern regarding cancer demonstrated in the debates on the 1938 amendments to the Act, see e.g., 79 Cong. Rec. 5023 (1935) (remarks of Sen. Copeland); 83 Cong. Rec. 7786-89 (1938) (remarks of Rep. Phillips and Rep. Lea). See also *Durovic v. Richardson*, 479 F.2d 242 (7th Cir. 1973), *cert. denied*, 414 U.S. 944.

ered by the Food and Drug Administration to be inseparable from consideration of the drug's effectiveness. The provisions of the bill are in no way intended to affect any existing authority of the Department of Health, Education, and Welfare to consider and evaluate the effectiveness of a new drug in the context of passing upon its safety.<sup>19</sup>

Language in the debates on the 1962 Drug Amendments reflects an understanding that the Act would apply to experimental drugs used to treat "cancer in its last stages".<sup>20</sup> Senator Eastland, proponent of the bill, also assumed that drugs administered for "fatal diseases, such as cancer," would be subject to the Act's requirements, noting that approval of such drugs would be appropriate even though they might only prolong life or alleviate suffering.<sup>21</sup>

In view of this Court's interpretation of the amendments to the Act as progressively strengthening and extending that law's protection of the consumer,<sup>22</sup> and the continuing evidence of concern by Congress with diseases that were considered "fatal", the protection afforded terminally ill patients under the Act has even greater force and effect today.

The plain language of the Act,<sup>23</sup> its legislative history

<sup>19</sup> Drug Amendments of 1962, Senate Report No. 1744, July 19, 1962, 1962 U.S. Code Congressional & Administrative News at 2891-2892.

<sup>20</sup> 108 Cong. Rec. 17399 (1962) (remarks of Sen. Kefauver, Chairman of the committee reporting the bill).

<sup>21</sup> 108 Cong. Rec. 1740 (1962) (remarks of Sen. Eastland).

<sup>22</sup> See e.g., *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 793-99 (1969); *United States v. Sullivan*, 332 U.S. 689, 697 (1948); *United States v. Dotterweich*, 320 U.S. 277, 280-82.

<sup>23</sup> Section 201(p), 21 U.S.C. § 321(p) of the Food, Drug and Cosmetic Act provides in part:

[Footnote continued on page 18]

set forth above, the holding of this Court that the Act is to be given a liberal construction<sup>24</sup> and should not be narrowed in coverage "short of the point where Congress indicated it should extend",<sup>25</sup> all point out the error inherent in the court of appeals' decision which carved out an exception from the Act for terminally ill patients. The court has usurped the role of the Congress by re-writing the Act. The departure of the court of appeals from the role of the judiciary parallels a similar departure noted by this Court in *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969):

The historical expansion of the definition of drug, and the creation of a parallel concept of devices, clearly show, we think, that Congress fully intended that the Act's coverage be as broad as its literal language indicates—and equally clearly, broader than any strict medical definition might otherwise allow. Strong indications from legislative history that Congress intended the broad coverage the District Court thought "ridiculous" should satisfy us that the lower courts erred in refusing to apply the Act's language as written. But we are all more convinced that we must give effect to congressional intent in view of the well-accepted principle that remedial legislation such as the Food, Drug and Cosmetic Act is to be given a liberal construction consistent with the Act's overriding purpose to protect the

<sup>23</sup> [Continued]

The term "new drug" means—(1) any drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use and under the conditions prescribed, recommended or suggested in the labeling thereof.

<sup>24</sup> *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 at 798. And see *United States v. Lee*, 131 F.2d — (7th Cir. 1942).

<sup>25</sup> 394 U.S. at 801.

public health, and specifically, § 507's purpose to ensure that antibiotic products marketed serve the public with "efficacy" and "safety." Cf. *United States v. Sullivan*, 332 US 689, 693-695, 92 L Ed 297, 301, 302, 68 S Ct 331 (1948); *United States v. Dotterweich*, 320 US 277, 283-284, 88 L Ed 48, 52-53, 64 S Ct 134 (1943).

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**C. The District And Appeal Court Decisions Conflict Markedly With the Decisions of Other Tribunals Presented With Patient Class Challenges To the Federal Drug Laws And Border on Pre-Emption**

The Court of Appeals' conclusion "as a matter of law that the 'safety' and 'effectiveness' terms used in the statute have no reasonable application to terminally ill cancer patients, and have no established meaning when considered in that context"<sup>26</sup> is in conflict with *Rutherford v. American Medical Association*, 379 F.2d 641 (7th Cir. 1967), cert. denied, 389 U.S. 1043<sup>27</sup> and also with *Tutoki v. Celebrezze*, 375 F.2d 105 (7th Cir. 1967).<sup>28</sup>

The *Allen Rutherford* case involved an action for a permanent injunction against the FDA and others by a physician and a number of cancer patients requiring that agency and others to cease their interference with the distribution, for their use, of the alleged cancer drug krebiozen. Krebiozen had not received new drug approval from the FDA and hence was unavailable in interstate commerce. The Court of Appeals "sympathetically viewed" the action as "an outcry of hopeless, suffering cancer victims." 379 F.2d. at 642. However, the Court

<sup>26</sup> Petitioners Appendix at 3a.

<sup>27</sup> Hereinafter referred to as the "Allen Rutherford" case to distinguish it from the Glen Rutherford case which is the subject of this proceeding.

<sup>28</sup> Hereinafter referred to as "Tutoki".

did not reach the conclusion that the Act does not apply to such "hopeless" cancer victims. It rather, in denying their claim for injunctive relief, held that the right to such relief requires a showing under the Act that under the procedures established by Congress for the introduction of new drugs, the drug Krebiozen would be approved or exempted (grandfather clause application) by the FDA.

In the *Tutoki* case, the court of appeals was asked to issue a declaratory judgment that the approval and exemption provisions of the federal laws relating to food and drugs do not apply to cancer patients and the drug they sought,—Krebiozen. 375 F.2d at 106. The *Tutoki* Court, specifically faced with the issue whether the federal drug laws were appropriately applied to cancer patients, mirrored the conclusions of the *Allen Rutherford* court,—that the FDA procedures cannot be bypassed unless it can be shown that the FDA, if it acted upon Krebiozen, who would have approved or exempted the drug.

The *Allen Rutherford* and *Tutoki* opinions thus postulate the provisions of the drug laws as applying to "hopeless" cancer patients,—the exact opposite of the result urged by the *Glen Rutherford* Court of Appeals.

A further ground for the reversal of the appeals court decision and adoption of the Commissioners decision lies in the nature of pre-emption. The impermissible conflict of the decisions of the district and the appeal courts with the federal drug laws. The legislative, administrative and court related history of the federal drug laws and amendments specifically articulate Congress' interest in protecting those with life-threatening illness or progressive (terminal) illness from drugs that are unsafe and ineffective. The *Rutherford* district court's certification of this case as a country encompassing class action, the legalization of laetrile in 19 states, the sham nature of the

affidavit system which permits those on the threshold of treatment easy access to a drug that has not satisfied recognized uniform standards of safety and efficacy all stand as obstacles to the accomplishment and execution of the full purpose and objectives of Congress in the establishment of uniform standards for drug access. *Cf. Ray v. Atlantic Richfield Co.*, — U.S. —, 55 L.Ed2d 179 (1978). A substantial amount of legislative history exists as early as the original 1906 Act of which the passage quoted below is representative, indicating an intent on the part of Congress that the federal drug laws establish uniform standards. Senator McCumber, a co-sponsor of the Senate bill states:

Another object is to prevent the evil of diverse rulings of the several commissioners of the States having pure-food laws . . .

We well know, Mr. President, that the moment we do pass a general law upon this subject, by virtue of that law covering ninety-odd percent of all of the commerce in impure products, that law must become the dominant law; and, if there is any difference, the State laws will soon accommodate and modify themselves in conformity with the national legislation.

40 Congressional Record 1216 (1906) See e.g., 21 U.S.C. § 355 (new drug provisions) and compare with Section 202 of Public Law 87-781 which provides that the 1962 Amendments of the Federal Food, Drug and Cosmetic Act invalidates any provision of state law that is in "direct and positive conflict" with the Act.

It is well settled that a state is permitted to legislate or regulate with a view to the protection of its citizenry against fraud or imposition by impure or ineffective drugs. However, it is equally well settled that a:

. . . state may not, under the guise of exercising its police power or otherwise, . . . enact legislation in



conflict with the statutes of Congress passed for the regulation of the subject, and if it does, to the extent that the state law interferes with or frustrates the operation of the acts of Congress, its provisions must yield to the superior Federal power given to Congress by the Constitution.

McDermott .. Wisconsin, 228 U.S. 115, 131-132 (1912) (citations omitted).

The pre-emption rationale applies not only to states but also, to the orders of federal district courts. See rationale of Judge Chapman in his Order of November 30, 1976 in re *Julian H. Morgan, Sr. et al. v. David Matthews, et al.*, Civil Action No. 76-1636, United States District Court of South Carolina, Spartanburg Division (appended hereto as Appendix A). The plaintiff cancer patients in the *Morgan* case, paralleling relief granted in some states by statute, sought to obtain civil, criminal and ethical immunity for physicians, nurses and technicians who would be administering laetrile. The plaintiff patients also sought a preliminary injunction restraining the federal officers from interfering with their procurement of a supply of Laetrile. In holding that the plaintiff cancer patients had not met their burden of satisfying the four criteria essential to the relief sought, Judge Chapman held that:

Finally, it has not been shown that the granting of injunctive relief in this case would not injure other parties or the public. To the contrary, to permit the distribution of Laetrile in this case would be to circumvent the laws enacted to assure that drugs distributed in interstate commerce be both safe and effective for their recommended use, and would undermine the ability of those charged with upholding these laws to do so most effectively in the future. Such a holding would also provide any future proponent of unproven remedies a basis for arguing to another court that it should allow the

*distribution of substances in a manner contrary to the law.* Appendix A at p. 6 (emphasis added).

**D. The Harm Perceived To The Allegedly Terminal Patient By Withholding An Exemption From The Federal Drug Laws For Laetrile Is De Minimus Measured Against The Substantial Harm To The Class Protected By The Act Particularly Those Whose Cancer Is Merely Life-Threatening**

Judge Chapman of the United States District Court for the District of South Carolina in *Julian H. Morgan, Sr. et al. v. Matthews, et al.*, Civil Action No. 76-1637, Order of November 30, 1976 (Appendix A hereto) denied a preliminary injunction sought by a person "suffering from the advanced stages of cancer of the prostate" to restrain federal officers from interfering with his procurement of Laetrile. He contrasted the lack of irreparable injury to the plaintiff cancer patient stemming from withholding access to laetrile with the injury to other parties and the public interest if the injunction were granted:

It has not been shown that the plaintiffs will suffer irreparable harm if the injunction is not forthcoming. The only evidence presented to this Court of any benefit Laetrile might provide in the treatment of cancer is that in some instances individuals taking it "seem to experience diminishing pain and an increase in appetite, weight gain, and psychological improvement." Affidavit of Raymond Hilliard, M.D. This is consistent with the effect a placebo would produce. The record is devoid of any evidence that Laetrile cures or halts the progress of cancer. Thus, it does not follow that the enforcement of a law which denies Laetrile to a victim of cancer will cause him to suffer irreparable harm.

\* \* \*

This Court is not unmindful of the gravity of the situation facing those who are afflicted with cancer and of their desire to choose their own remedies in

view of the absence of any known cure for this disease. However, granting the relief requested in this case could not only harm the public by weakening laws calculated to prevent the victimization of those afflicted with cancer and other conditions by playing on their desperation in the marketing of unproven and, possibly worthless remedies, but it could also further the growing tendency of those afflicted with this disease to engage in self treatment resulting in a delay in seeking early diagnosis and prompt treatment with forms of therapy that have no established value. The result of this type of delay could be disastrous, since early diagnosis and treatment is of the utmost importance in the management of cancer.

(Appendix A at pp. 5-7) (footnotes omitted).

Judge Chapman's concern that approval of laetrile for the terminally ill poses a substantial threat to those whose cancer is in a treatable stage is noted by Dr. Lewis Thomas at the Hearings held by Senator Kennedy on the Laetrile issue in July of 1977.<sup>30</sup>

It is often asserted that since Laetrile is not a particularly toxic substance, it should be made available to all patients who wish to use it as a matter of free choice. There is, however, a very real danger here. If, for example, children with early leukemia or sarcoma, or women with cancer of the breast, or young men with Hodgkin's disease, are persuaded to give Laetrile a trial before doing anything else, the outcome will almost certainly be death, in cir-

<sup>30</sup> Hearings Before the Subcommittee on Health and Scientific Research of the Senate Committee on Human Resources, "Evaluation of Information on which the FDA Based its Decision to Ban The Drug Laetrile From Interstate Commerce", 97th Cong., 1st Sess. 14 (1977).

cumstances where appropriate therapy could be life-saving.<sup>30</sup>

Similar objections to an exemption for the terminally ill were raised by David T. Carr, M.D. and made a part of the record in the Laetrile Rulemaking proceedings. Dr. Carr expresses his opinion concerning the medical and scientific basis for, and the public health consequences of the availability of amygdalin, or other similar unproven cancer remedies, for clinical use in patients with "terminal" cancer:

My opinion is that this would be unwise. The expression "terminal cancer" is a poor one. A patient may be critically ill due to the effects of a cancer and improve at least temporarily or even permanently following appropriate therapy. Administration of an ineffective drug such as amygdalin instead of such appropriate therapy would deprive a significant number of patients of their chance for some relief, temporary though it might be in many cases.

It is true that many patients come to a point in time when only supportive care is possible. It has been argued that administration of amygdalin to these patients would do no harm. No one knows whether or not the drug would do no harm. There

<sup>30</sup> Some examples of resort to laetrile by patients before resort to conventional therapy are in "Healing: A Doctor In Search of a Miracle", William A. Nolen, M.D. (Random House); Ad.R. 197, Donald C.S. Tan M.D. and the Report of the Alameda County Coroner on his investigation of a death by cyanide intoxication of a patient on laetrile therapy, Appendix B hereto at pp. 69-71.

The importance of early detection and treatment in terms of survival when cancer is localized as opposed to delay in treatment until the cancer has spread is set forth in the American Cancer Society's 1979 Cancer Facts and Figures at page 9. The chart shows the following five year survival rates for localized as compared to disseminated cancer: bladder 72/14; breast 85/47; colon-rectum 71/26; larynx 79/32; lung 33/4, oral 67/25, prostate 70/35, uterus-cervix 78/37 and uterus-corporis 86/33.

is no reason to believe that it would do any good. And if it were made generally available for that group of patients it would inevitably be given to or obtained by others for whom effective therapy is available. Once the decision is made to permit the distribution of one useless drug for such cases there will certainly be more proponents demanding that the same loophole in the law be open to their unproven remedy.<sup>31</sup>

Further, approval of laetrile for the terminally ill would give the appearance of an official imprimatur, and would encourage use of the drug by patients who could be helped by legitimate therapy. See the Commissioner's Opinion at Petitioner's Appendix p. 268a. James Harvey Young, a noted medical historian, testified on the basis of his study of past unproven cures that "[p]ermitting laetrile's use in terminal cases gives it a credence among the public at large that will expand its use in early cases, for people will prefer taking a 'vitamin' to confronting the surgeon's knife." Petitioners' Appendix at 269a. Dr. Samuel G. Klagsbrun, a psychiatrist who works with cancer patients at St. Luke's Hospital in New York, testified that "[p]ermitting laetrile to be used by any population of cancer victims would have the correlative effect of creating the misimpression in the minds of other cancer victims that the drug is, in fact, safe and effective for a broader population." Petitioners' Appendix at 269a.

<sup>31</sup> To the same effect see Ad.R. 191 at H6, the affidavit of Philip Schein, M.D.:

"If Laetrile is permitted in general clinical use without its effectiveness having first been demonstrated by substantial evidence, it will open a Pandora's box which will plague both the medical profession and the public for many years to come. The precedent would allow many other ineffective drugs to be used under the guise of effective placebo therapy or psychological support—in conditions for which there are not data to support their effectiveness."

The record of this proceeding makes highly visible the practical impossibility of restricting the importation of laetrile to the terminally ill. The obstacles to such restriction were attested to by an officer of the Drug Enforcement Administration one Kenneth Durrin, Acting Director of the Office of Compliance of the Drug Enforcement Administration. Mr. Durrin related the agency's experience in regulatory other controlled substances available for limited use, e.g., cocaine and then applied that experience to the Laetrile problem. He testified that since Laetrile does not appear to have a central nervous system effect, it would not come under the controlled substances act and the controls available under the Act. "Absent the kinds of controls available under the Controlled Substances Act—and indeed even with such controls—it is my opinion that a drug such as Laetrile could not effectively be restricted to a class of terminally ill cancer patients. For example, absent a quota on production, manufacturers would not be limited to producing an amount of Laetrile sufficient only to provide a source of supply for terminal cancer patients. Manufacturers would not be restricted in the channels in which they could permissably distribute the drug. They would not be required to report transactions in Laetrile." Ad.R. 435 at 7293.

The inability to restrict usage also flows from the practical impossibility of arriving at an objective standard that will not lend itself to abuse. See discussion at pp. 7-10, *supra*.

Both the potential for and actuality of abuse is apparent from the record before the court of appeals. Food and Drug Administration investigators telephoned patients who had executed patient importation affidavits in the district court proceeding. A common pattern emerged. The need of patients whose six month laetrile requirements were 26 ampoules and 180-185 tablets were



stated by affidavit without their permission to be 150 ampoules and 750 tablets. The excess is apparently used by the "importer" to supply patients who had not executed affidavits. See Ct.R. 409-414, 423-480 and see Ct.R. 1505 and attachments. This type of abuse resulted in a complaint for forfeiture before the district court in Maryland<sup>32</sup> to seize from a pharmacist acting as agent for patients holding laetrile import affidavits the laetrile procured by him which exceeding their actual orders:

4. As agent for the persons named in the affidavits, Mr. Henderson was authorized to deliver to these persons the amounts of Laetrile imported on their behalf and for their personal use.

5. Investigations by United States Food and Drug Administration investigators have revealed that the affidavits are fraudulent in that patients on whose behalf affidavits were presented to customs officials either ordered significantly less than the amount of Laetrile declared on the affidavits or did not order any Laetrile whatsoever and are unaware of any affidavit being executed on their behalf.

6. Food and Drug Administration investigations further reveal that Mr. Henderson has solicited abandonment of Laetrile from patients who ordered Laetrile and on whose behalf affidavits were presented to customs officials and that either as a result of such solicitations or for other reasons, some patients have cancelled or reduced their orders for Laetrile.

7. Food and Drug Administration investigations further reveal that affidavits presented to customs officials contain false information in that the amounts

<sup>32</sup> United States v. Articles of Drug . . . Amigdalina Cyto Pharma De Mexico, S.A., Docket No. K77-1283 filed on August 4, 1977. The complaint and Motion for Patient Release on Seized Goods and Supervised Delivery to Certain Patients are appended hereto as Appendix D.

of Laetrile represented to have been ordered by the patients exceeds the amounts actually ordered and that Mr. Henderson uses these amounts of Laetrile not ordered by patients to create a stockpile from which he then sells to other persons who have not executed affidavits presented to Customs for purposes of facilitating importation of the drug for their use.

A final example of abuse arises in a case involving a minor treated with chemotherapy under court order whose parents were also administering laetrile and other therapies to him without court permission. During a hearing on whether the child was harmed by the addition of laetrile, massive doses of vitamin A and enzyme enemas, a doctor testifying for the parents stated that he did not believe that the minor was terminally ill but that he would execute an affidavit such as that required by the district court in the case before this Court stating that the minor was terminal in order to permit the child to procure a supply of laetrile.<sup>33</sup>

The dangers posed by approval of laetrile for the terminally ill are particularly clear in the case of children with cancer. Children constitute only one percent of the cancer cases in this country but cancer represents the most serious threat to childlife next to accidents. Childhood cancers are also the category in which the greatest success in long-term remission and "cures" have been made. Yet, the natural desire for parents to avoid the suffering for their child which is a part of conven-

<sup>33</sup> In Custody of a Minor (Appendix C), Dr. Ernesto Contreras testified that the minor does not have terminal cancer. He also testified that despite the fact that the minor does not have terminal cancer, he would be willing to sign a "Bohanon affidavit" attesting that Chad does have terminal cancer. On the following day, Dr. Bruce Halstead of California made the same statement.

The record in this case is sealed until an appeal is taken. The information in text was received from a physician-witness for the State of Massachusetts.

tional treatment makes this class a minority which requires protection from the loophole in the law advanced in the *Rutherford* court appeal.

This need is illustrated by a recent Massachusetts case arising from a physicians request to have a child committed to the Department of Public Welfare for the purpose of providing necessary medical care (chemotherapy) for the treatment of leukemia. *Custody of a Minor*, S.J.C. No. P-1422, Mass. Supreme Court, Plymouth Division of April 18, 1978 in Civil Action No. 78-6916.

Indeed, given the nebulous benefits which can be anticipated by the truly terminal patient from access to laetrile, the court of appeals exemption deprives that class of patient of very real and needed protections stemming from the nature of end-stage disease which are secured to this class by the federal drug laws. The court of appeals asked the question:

[W]hat can "generally recognized" as "safe and effective mean to such persons who are so fatally stricken with a disease for which there is no known cure?"<sup>34</sup> What meaning can "effective have in the absence of anything which may be used as a standard. Under this record Laetrile is as effective as anything else. What can "effective mean if the person, by all prevailing standards, and under the

<sup>34</sup> This finding flies in the fact of administrative and court interpretation which has hitherto consistently found the Act and its safety and effectiveness provisions applicable to cancer patients. See e.g., Hearings on S. 1552 Before the Subcomm. on Antitrust and Monopoly of the Senate Comm. on the Judiciary 87th Cong., 1st Sess. Part 5, at 2588 at which the Secretary of HEW explained the FDA's attitude as follows: "If the drug is offered for the treatment of progressive or life threatening diseases such as cancer, or if the drug is seriously toxic or has alarming side effects we now consider its effectiveness." (emphasis added). See also, *Durovic v. Richardson*, 479 F.2d 242 (7th Cir. 1973), cert. denied, 414 U.S. 944, and the decision at pp. 15-18, *supra*.

position of the Commission takes, is going to die of cancer regardless of what may be done. (Petitioner Appendix at 6a).<sup>35</sup>

The Court of Appeal's focus is apparently restricted to "cure" and is thus too narrow in terms of the class it addresses,—the terminally ill. Bernard C. Meyer in an article "Truth and the Physician" reprinted in *Ethical Issues in Death and Dying* (1977) at 533, observes that the "Physician's response once he can no longer arrest disease is to assuage discomfort and distress". A cure may not be possible, but other relief for the terminally ill may be, for example, pain control, appetite stimulation, tranquilization.

In the Laetrile Hearings it became clear that the purveyors of laetrile have moderated their claims for the substance in recent years. For the most part, it is no longer openly claimed<sup>36</sup> that laetrile cures cancer [although this is the expectation of the cancer victims that turn to it].<sup>37</sup> The current thrust of the laetrile

<sup>35</sup> There is inconsistency in the Court of Appeals finding that the terminally ill are excluded for the strictures of the Act while at the same time confining the utilization of laetrile to an injection route.

<sup>36</sup> Compare the remarks of Lewis Thomas, M.D., Director of the Memorial Sloan-Kettering Cancer Center at Laetrile Hearings pp. 13-14 ("It is no longer openly claimed that Laetrile cures cancer", although some of the leaflets and public releases hing broadly in this direction.") with the remarks of Senator Kennedy at p. 257: "... the thing that's interesting about your careful choice of words about the impact of this [Laetrile] would be you had no reluctance of using the word 'cures' or 'recoveries' in the transcripts here before the California case. It was a tape of the town meeting. And I'll just read: 'Some cases have undergone clinical arrests, or for other practical purposes, we might describe as cures or recoveries.'"

<sup>37</sup> See Record Volume XIV, Transcript on Plaintiffs Motion For Temporary Injunctive, July, 1975, Ct.Tr. 6 ("Laetrile . . . has completely neutralized his . . . cancer"); 7. ("cancer victors' . . . have been denied what many, many physicians and high level biochemists feel is a complete cancer remedy. Nothing is complete, but I

proponents seems to be that it will dramatically relieve pain, improve appetite, promote weight gain, reduce the odor associated with cancer, improve the cancer patients general sense of well-being, control or prevent cancer.<sup>38</sup>

The terminally ill are entitled under the Act to the assurance that the products they seek to use are effective not only for cure or treatment but also for these other purposes.

Cancer victims constitute a minority group in our society; terminal cancer patients constitute an even smaller minority, but like other groups, they have a right not to be exploited. In the case of cancer drugs, particularly the exercise of government power of protection, premarket clearance is not only reasonable, but necessary to protect the compelling public interest in effective cancer therapy, and in assuring that non-therapeutic drugs do what they say. In view of the widespread incidence of cancer, the serious consequences of the disease, the expe-

mean a very effective remedy); 30 ("I am alive because of it"). 86 ("I hope and pray that we will get his protective order to keep him alive.")

<sup>38</sup> See e.g., Laetrile Hearings at pp. 13-14 (Dr. Thomas). 246-247, 271-72 (prevention, control, pain relief, appetite increase, weight gain, feeling of well-being), J.A. Richardson, M.D. physician using laetrile, 295-297 (stimulation of appetite, weight gain, decrease or eliminate pain, bad odor, pallor, remarks of Robert Bradford, Committee on Free Choice for Cancer Treatment. Mr. Bradford also stated at p. 295 that "Laetrile is not offered as a cancer cure. There is no cure for cancer . . . In the very best of instances it may effect a control—but not a cure—of cancer . . ."). See also the opinion of the Commissioner of the FDA at Petitioners Appendix pp. 73a-78a.

Compare the Alameda County Coroner's Report, Appendix B hereto at 17a in which a patient with advanced carcinoma of the breast who was on laetrile treatments. The medical report furnished to the Coroner from the laetrile clinic at which she was treated since March of 1978 referred to her complaints of "loss of sleep associated with severe pain." She died of cyanide intoxication in December of 1978.

rience with the particular vulnerability of cancer patients and their families to promoters of easy money-making schemes labeled in mysterious scientific dress, it is imperative that the standards of consumer protection set forth in the federal drug acts be maintained.

Further, the Court of Appeals assumes that Laetrile by injection is safe.<sup>39</sup> This assumption is unsupported by the record before this Court. An awareness of the actual and potential toxicity of Laetrile has emerged in recent expressions of scientific opinion.<sup>40</sup> Of particular significance is the article "Laetrile Toxicity: A Report of Two Cases", Smith and Schein, 238 Journal of the American Medical Ass'n 1361 (Sept. 1977). This article describes a case of serious side effects relating to administration of laetrile by injection and the cessation of such side effects when the laetrile was withdrawn.

<sup>39</sup> The Court of Appeals direction to the FDA to promulgate regulations relating to the use of laetrile by injection by the terminally ill, cannot be executed. The laetrile proponents have been unable to provide a consistent picture of what the components of laetrile are. The samples alleged to be laetrile seized and analyzed by the FDA have had differing chemical compositions. Specifically, Commissioner Kennedy testified at pp. 4-5 of the Laetrile Hearings that the substance "has no fixed identity in the hands of our analytical chemists who find that the amount of amygdalin and the ratio of its isometric forms varies widely in the samples of materials we had seized." See also the Commissioners Opinion at Petitioners Appendix pp. 182a-187a.

Compare, *Durovic v. Richardson*, 479 F.2d 242, 251 (7th Cir. 1973), cert. denied, 414 U.S. 944. In that case, the Court of Appeals, as one rationale for its decision that Krebiozen could not be generally recognized as safe even in the narrow sense of non-toxic by qualified experts found that as of "October 9, 1962, the identity and composition of Krebiozen was completely unknown."

<sup>40</sup> See e.g., Jukes "Laetrile for Cancer" 236 Journal of the American Medical Ass'n 1284 (1976); Lambert, "Fatal Cyanide Poisoning: Accidental Ingestion of Amygdalin," 238 Journal of the American Medical Ass'n 482 (1977) and Lewis, "Laetrile" 127 Western Journal of Medicine 55 (1977); and the toxicity issue is discussed at pp. 59-71, *infra*.



## II. APPLICATION OF THE APPROPRIATE BURDEN OF PROOF AND REVIEW CRITERIA DEMONSTRATES THE DISTRICT COURT'S ERROR IN FINDING AN EXEMPTION FOR LAETRILE UNDER THE 1962 GRANDFATHER CLAUSE FROM THE SAFETY AND EFFICACY REQUIREMENTS OF THE FEDERAL DRUG LAWS AND SUPPORTS THE COMMISSIONER'S FINDING THAT NO EXEMPTION IS WARRANTED

### A. Standards of Proof and Review Criteria

No matter how a drug becomes the subject of an FDA rulemaking proceeding—agency initiative, manufacturer or other drug proponent initiative, court referral—the burdens of proof and proceeding and the standards of review established by the federal drug laws as construed by the courts are the same. The statute and regulations do not require the Food and Drug Administration to prove a drug ineffective but rather, the burden of proceeding and proof of safety/efficacy by a substantial amount of well documented evidence lies with the proponents of the drug.<sup>41</sup> The court of appeals and the district court below, from the outset, have eschewed the statutory standard and have created a hybrid standard. The standard literally requires the FDA to initiate an administrative proceeding on drug status and bear the burden of proof in that proceeding whenever, in the absence of an administrative record or new drug application, the FDA proceeds with the presumption of "new drug" status. As stated by the Court of Appeals:

We are unable, however, to see how the FDA can escape the obligation of producing an administrative record to support its determination of the first and

<sup>41</sup> See e.g. *Weinberger v. Hynson, Westcott and Dunning, Inc.*, 412 U.S. 609, 617 (1973); *Ubiotica Corp. v. FDA*, 427 F.2d 376, 378 (6th Cir. 1970); *Upjohn Co. v. Finch*, 422 F.2d 944, 955 (6th Cir. 1970); *North American Pharmacal, Inc. v. HEW*, 491 F.2d 546, 550-51 (8th Cir. 1973).

more fundamental issue that Laetrile is a new drug, for it is not a new drug merely because they say it is. . . . To support its determination the FDA in the case at bar would have to present substantial evidence to support the proposition that Laetrile is not generally recognized among qualified experts as "safe and effective," and that Laetrile is not grandfathered by either of the exemptions discussed above.<sup>42</sup>

The FDA is not required by any provision in the federal drug laws or any principle of administrative law to initiate a rulemaking proceeding to determine the "new drug" or "grandfather" status of a product before the agency can declare that product to be a "new drug." 42 Federal Register 10067 (1977). For example, the predicate of each enforcement action which the agency brings to prevent and punish violations of 21 U.S.C. §§ 331(d) and 355(a) is the "new drug" status of the product involved. The decision made to initiate enforcement proceedings is technically based on probable cause that a drug is in violation of the Act.<sup>43</sup> The absence of an "approval" or "exemption" in its records that the FDA can point to requires a "new drug" description until the proponents of the drug have proven differently.

A reversal of burdens of proof and proceeding when an affected patient requests relief conflicts with the decisions in other courts. For example, District Court Judge Chapman in *Julian H. Morgan Sr., et al. v. David Matthews, et al.*,<sup>44</sup> denied the same relief request by the patient plaintiffs in *Rutherford* with the following rationale:

Plaintiffs apparently contend that the burden is on the FDA to approve or disapprove of a new

<sup>42</sup> 542 F.2d at 1143 and Petitioners Appendix at 32, 13a nn.3-4, 14a n.5.

<sup>43</sup> See *Ewing v. Mytinger & Casselberry, Inc.*, 339 U.S. 594 (1950).

<sup>44</sup> Appendix A hereto.

drug in the first instance, since they complain that the FDA "has failed, without adequate explanation, to approve Laetrile for distribution and use in the United States. . . . "The language and history of the Act demonstrate that it is not the responsibility of the FDA to initiate applications on its own in the absence of an application that conforms with the statutory requirements of § 505(a) and (b). No such application has been filed here. See Finding of Fact 2, *supra*.

The FDA has been given the responsibility of "approving applications". Therefore, it is apparent that they must be submitted for approval. This conclusion conforms with the Act's legislative history.

The House Committee Report discussion § 505 during its initial drafting in 1938 stated that

This provision will not put the Federal Government into the business of developing new drugs, nor will it require the Government to duplicate laboratory and clinical tests made by responsible manufacturers. The provision merely sets up a method for the authoritative review of the manufacturer's tests and will not unreasonably delay the introduction of new drugs in the market.

H.R. Rep. No. 2139, 75th Cong., 3rd Sess. (April 14, 1938), p.9. Further discussion was held as to this section in the House Report of 1962 amended version, which indicates that application was to be made by the manufacturer:

Section 505 of the Food, Drug and Cosmetic Act prohibits interstate shipment of a "new drug" . . . unless it is first cleared for safety through the filing of a new drug application by the manufacturer.

H.R. Rep. No. 2464, 87th Cong., 2d Sess. (Sept. 22, 1962), p.3 <sup>45</sup>

Further, Judge Kiley, in *Tutoki v. Celebrezze*, 375 F.2d 105 (7th Cir. 1967) denying declaratory relief against the FDA to cancer patients seeking Krebiozen because of their failure to exhaust administrative remedies, expressly found that the statute did not preclude cancer patients from sponsoring an NDA for Krebiozen. Finally, Judge Hastings speaking for a unanimous court in *Rutherford v. American Medical Ass'n et al.*, 379 F.2d 641 (7th Cir. 1967), found as one basis for his decision that the FDA need not cease its interference with patient/physician procurement of Krebiozen, that the Krebiozen proponents had not shown that they had made a good-faith attempt to comply with the procedures established by Congress for the introduction of new drugs. The court reasoned as follows:

In their complaint, plaintiffs have alleged, in effect, that the FDA has systematically attempted to discredit Krebiozen and to prevent its introduction into commerce. It is argued that on a motion to dismiss, we must accept the truth of these allegations.

Accepting their truth arguendo, plaintiffs still have not shown that they have in good faith attempted to comply with the procedures established by Congress for the introduction of new drugs, nor has it been shown that the failure to apply can be attributed solely to the activities of the FDA and the defendants. The fact that compliance might be expensive and burdensome, is not unfairness in the procedure, but a consequence of a reasonable Congressional scheme for the introduction of new drugs.

Without an attempted good faith application for approval or exemption, we have no jurisdiction to de-

<sup>45</sup> *Id.* at page 5.

termine whether the FDA has illegally placed impossible or unreasonable conditions on approval or exemption, or has made requests for information impossible to fulfill, or whether the FDA has been dilatory, biased, or discriminatory. Until someone has attempted to comply with the Act with respect to Krebiozen, plaintiffs' appeal should be to the sponsors of the drug.<sup>46</sup>

Thus in parallel cases, courts have held that the shift of proponent position from manufacturer/developer to patient permitted no dilution of the standards and procedures for determination of the status of the drug.

Deviation from the prescribed statutory standard of proof is also inconsistent with the relative positions of the parties in this proceeding. The "evidence" which the FDA is supposed to provide lies within the control of those physicians and manufacturers who are said to be using and making Laetrile. This is not an enforcement proceeding in which the Government by seizure/subpoena or other process can "require" the production of evidence. The record in the Laetrile Rulemaking proceeding is clear that the proponent manufacturer/developers of the drug have not made a good faith attempt to comply with the NDA or IND procedures. They submitted applications in 1962 and 1970 but when notified of deficiencies did not come forward with submissions conforming with statutory and regulatory criteria to correct those deficiencies.

No attempt was made by the proponent manufacturers/developers in the rulemaking proceeding to utilize this opportunity to come forward with the quantity and quality of proof to support approval of a "new drug." One conclusion that may be drawn from this factual scenario is that the manufacturer/developers of Laetrile

<sup>46</sup> 379 F.2d at 643.

are utilizing the cancer patient as a pawn to effect an end run around the provisions of the provisions of the federal drug laws.

The statute and case law both sustain the proposition that the burden of proceeding and providing evidence that will sustain the substantial evidence tests imposed by the federal drug laws for the admission of a "new drug" to interstate commerce, lies with the Laetrile proponents. The only issue involved in the decisions below which concerns the presence or absence of such substantial evidence<sup>47</sup> is the district court's finding that the 1962 grandfather clause is applicable. This presents an alternative ground for or reversal or affirmance of the court of appeals decision by this Court.<sup>48</sup> Entitlement to the grandfather exemption of the 1962 amendments, i.e. Section 107(c)(4) of the Food and Drug Act,<sup>49</sup> is limited to drugs which:

1. feature *today* the identical chemical composition recommended dosages, and claims made in labeling as existed on October 9, 1962, *and*
2. were used or sold commercially in the United States on October 9, 1962, *and*
3. were generally recognized by the experts as safe; *and*

<sup>47</sup> See *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609, 632 (1973).

<sup>48</sup> The district court apparently concedes Laetrile's status as "drug" (Petitioners Appendix at 18a) and its inability to meet the "efficacy" standards of the Act (Pet. App. at 22a), thus the "exemption" of laetrile from new drug status by application of the 1962 grandfather clause (Pet. App. 25a) is the alternative grounds for affirmance which involves the scrutiny of the record and allocation of burden of proof.

<sup>49</sup> Pub. L. 87-781, found as a note to 21 U.S.C. § 321. Section 107(c)(4) is quoted in full in the statutory appendix hereto.



4. were not covered by an effective drug application.<sup>50</sup>

The grandfather clause exception to the federal drug laws is construed strictly against those invoking it.<sup>51</sup> The failure of a drug to meet just one of these criteria extinguishes altogether its entitlement to grandfather status. The record in this proceeding clearly demonstrates that laetrile fails to meet each and every one of the four criteria.

The remanding opinions and orders recognized the "primary jurisdiction" of the FDA to determine the "status" of a drug and directed that the determination be made via a rulemaking proceeding.<sup>52</sup> The FDA acted. The resulting Commissioner's decision is subject to the standards of the court scrutiny applicable to review of agency action. The review court is required to view the record as a whole<sup>53</sup> and determine whether the Commissioner has articulated the grounds of his decision, whether those grounds are consistent with the statute, and whether

<sup>50</sup> *United States v. Allan Drug Corp.*, 357 F.2d 713, 718-19 (10th Cir. 1966), *cert. denied*, 385 U.S. 899; *United States v. 1,048,000 Capsules, More or Less*, 347 F. Supp. 768 (S.D. Tex. 1972); see also *Rutherford v. United States*, 542 F.2d 1137, 1141 (10th Cir. 1976). The Commissioner concedes issue No. 4 in the Notice of Rulemaking and it need not be addressed here.

<sup>51</sup> See e.g., *United States v. Allan Drug Corp.*, 357 F.2d 713, 718 (10th Cir. 1966), *cert. denied*, 385 U.S. 899 (1966). *Accord Durovic v. Richardson*, 479 F.2d 242, 250 n.6 (7th Cir. 1973), *cert. denied*, 414 U.S. 944; *United States v. An Article of Drug . . . Bentex Ulcerine . . .*, 469 F.2d 875, 878 (5th Cir. 1972), *cert. denied*, 421 U.S. 938 (1973); *United States v. 1,048,000 Capsules, More or Less, et al.*, 347 F. Supp. 768, 770 (S.D. Tex. 1972), *aff'd* 494 F.2d 1158 (5th Cir. 1974).

<sup>52</sup> *Rutherford v. United States*, 542 F.2d at 1143-1144 and *Pet. App.* at 12a.

<sup>53</sup> See the Administrative Procedure Act 5 U.S.C. Section 706, and see *Diamond King Ranch, Inc. v. Morton*, 531 F.2d 1397, 1405 (10th Cir. 1976).

those grounds are supported by the evidence of record. In short, if the Commissioners decision shows that the FDA has a reasonable basis for concluding that the drug proponents submissions did not comply with the substantial evidence requirements of the statute and regulations; the Commissioner's decision should be affirmed.<sup>54</sup> As the 10th Circuit itself has indicated:

Review under this provision of the A.P.A. provokes inquiry whether the administrative decisions were based on a consideration of all the relevant factors and whether there was a clear error of judgment. *Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 416, 91 S.Ct. 814, 28 L. Ed2d 136. Although this inquiry into the facts is to be searching and careful, the ultimate standard of review is a narrow one. The court is not empowered to substitute its judgment for that of the agency. *Id.* The court's function is exhausted where a rational basis is found for the agency action taken. *Udall v. Washington, Virginia and Maryland Coach Co.*, 130 U.S. App. D.C. 171, 398 F.2d 765, 769, *cert. denied*. *Washington Metropolitan Area Transit Com. v. United States*, 393 U.S. 1017, 89 S.Ct. 620, 21 L.Ed2d 561.

Application of the proper standard of proof and review criteria supports the conclusion reached by the Commissioner, detailed below, that the drug Laetrile does not satisfy any of the elements of the 1962 grandfather clause.

<sup>54</sup> *Sabin v. Butz*, 515 F.2d 1061, 1067 (10th Cir. 1975).

**B. Laetrile Is Not Entitled To Grandfather Status Because Its Chemical Composition And Recommended Conditions For Use And Administration Are Not The Same Today As They Were On October 9, 1961<sup>55</sup>**

**1. The Relationship Between Laetrile and Amygdalin**

Laetrile is the term used to describe a class of cyano-genic glucosides of which the substance amygdalin is the primary ingredient.<sup>56</sup> The terms amygdalin and Laetrile are often used interchangeably. This stems from the fact that amygdalin is the one ingredient which in varying percentages has been consistently present in the "laetriles." However, this interchangeable use is incorrect.<sup>57</sup> Laetrile and amygdalin differ in formulae and

<sup>55</sup> The variations in composition and conditions of usage for the drug Laetrile are set forth graphically in the time line flow chart at pp. 65-68 of this brief. The chart by years from 1920's through 1978 represents the claims made by Laetrile's mechanism (rational) of drug action, label/pamphlet claims, formulation, method of preparation (reconstitution), dosage, route (method of) administration, use as an investigational drug which is inconsistent with claims of commercial marketing and the representations as to safety and toxicity made Laetrile labels and pamphlets.

<sup>56</sup> See Dorr, Paxinos "The Current Status of Laetrile," 89 Annals of Internal Medicine 389 (1978) (hereinafter "Annals"). See also, Korbitz, Ad.R. 181 at 195E, "Laetrile is a somewhat crude preparation of amygdalin."

<sup>57</sup> See e.g., Annals supra at 389. See also Harold W. Manner, Ph.D., at R262 and W. Sherwood Lawrence, M.D., at Ad.R. 183 at p. 7; Opinion of the Attorney General of Illinois "Public Health: Interpretation of Act Allowing Giving of Amygdalin or 'Laetrile' to Terminal Cancer Patients, File No. S-1331, January 15, 1978 ("Amygdalin" and "Laetrile" (illegible) separated and interchangeably in the statute; amygdalin has an accepted scientific chemical formula and "Laetrile does not; The statute intends "Laetrile" as covered by the statute "when its active ingredient is amygdalin."); See also Markle, Peterson & Wagenfeld, "Notes From the Cancer Underground: Participation in the Laetrile Movement" 12 Social Science & Medicine 31, 37n (1978) (There is some doubt

also in chemical structures.<sup>58</sup> "Under British patent 788,855 (1958) Laetrile is described as 1-mandelo nitrile-beta-glucuronic acid and differs from amygdalin by the absence of the second glucose moiety present in tandem in the readily available amygdalin." The Commissioner in his rulemaking decision correctly recognized the distinctions between the substances. See Pet. App. at 58a-70a.<sup>59</sup>

**2. The Record On The Chemical Composition And Conditions Of Use For Laetrile**

The record in the rulemaking proceeding fully supports the Commissioners determination that Laetrile is not a compound which has enjoyed any continuity of composition or recommended conditions of use and administration. See Pet. App. at 58a-73a, 182a-204a. By way of contrast, the district court (Pet. App. at 25a-34a) exempts Laetrile by application of the 1962 grandfather clause, but does not address any of the issues in-

that Laetrile and amygdalin are, in fact identical substances). Ct.R. 1507 "Amygdalin (Laetrile) Therapy, 1977, Bruce Halstead, M.D. This booklet was plaintiffs exhibit before the district court. At page 3 of the booklet, Dr. Halstead, a laetrile advocate, states: "The terms amygdalin and Laetrile are frequently used interchangeably by laymen, but are not chemically synonymous."

<sup>58</sup> See Annals at 390; Fenselau "Mandelonitrile B-Glucuronide: Synthesis And Characterization, 198 Science 625, 626 (1977); Pet. App. 60a-64a and Ct.R. 1507 supra note at pp. 4-5. The amygdalin chemical formula is expressed as d-mandelonitrile-B-D-glucoside-6-B-D glucose and its structure is represented as  $C_{20}H_{27}NO_{11}$ . The Laetrile chemical is usually expressed as laveo-mandelonitrile-B-glucuronic acide or  $C_{14}H_{15}NO_7$ .

<sup>59</sup> The significance of the distinctions between Laetrile and amygdalin arises from the arguments made by the laetrile proponents below and echoed by the district court (Pet. App. at p. 26a-34a) that if Laetrile and amygdalin are interchangeable, amygdalin availability as a chemical from drug supply houses satisfies the commercial marketing requirements of the 1962 grandfather clause. The fallacy of this argument is discussed in text at pp. 54-56, *infra*.

herent in the labeling/conditions of use arm of the grandfather provision: Drug formulation, consistency, dosage, route of administration, theory of action and claims for the product now and prior to October 9, 1962.<sup>60</sup> With one exception,<sup>61</sup> the only reference to chemical formula made by the district court relates to amygdalin (Pet. App. at 34a n.24) not laetrile. See discussion on interchangeable use at pp. 42-43, *supra*.<sup>62</sup>

Table A at pp. 65-68, *infra*, demonstrates the lack of consistency and predictability as to method of action, chemical formula, dosage, route of administration, claims for use as well as safety and toxicity and the absence of commercial marketing data in the record. This is the

<sup>60</sup> Since all grandfather criteria must be met before an exemption is applicable, this deficiency alone nullifies the district court's finding of an exemption. See note 51 *supra*, and *United States v. Bentex Ulcerine*, 469 F.2d at 878.

<sup>61</sup> The district court's sole reference to Laetrile's formula is at note 17 at Pet. App. 26a. The district court attempts to explain away the obvious differences between a specific laetrile and amygdalin formula by referring to R.183 at which Mr. Krebs stated that he had abandoned that specific synthesis of laetrile because it was too expensive to formulate. The district court makes no attempt to explain the many other differences in laetrile versus amygdalin formulae. See e.g. Ad.R. 183, Attch. 16 at pp. 27-28 (Laetrile = Sodium 1-mandelonitrile-beta-glucuronoside); Ad.R. 167 Exh. 2 at p. 143 (Laetrile = 1-mandelonitrile-beta-glucuronoside); and see the discussion in text and notes at pp. 42-43, *supra*. The articles in *Science* and the *Annals of Internal Medicine* diagram laetrile/amygdalin and show the differences in chemical formula.

<sup>62</sup> The district court attempts to dilute the effectiveness of the grandfather clause by construing it as exempting any drug "to the extent that it is currently being used for the same purposes and under the same conditions and labeling as on October 9, 1962." (Pet. App. at pp. 15a-16a, note 7). This construction flies in the face of *United States v. Allan Drug Corp.*, 357 F.2d 713, 718 (10th Cir. 1966) cert. denied, 385 U.S. 899. In that case, the court held that a drug relabeled by court order after 1962 to eliminate false claims was not entitled to a grandfather clause exemption. The Allan court "confine(d) the exemption to drugs intended solely for use under the conditions prescribed on the effective date of the Act" 357 F.2d at 719.

bedrock underlying the Commissioners decision that the elements of a grandfather exemption have not been supported by substantial evidence. The Table also demonstrates the error of the district court. By way of illustration, some of the inconsistencies in chemical composition and usage of the drug set forth in the Table are discussed below.

Laetrile traces its genesis to the work of Dr. E. T. Krebs, Sr. with amygdalin in the 1920's,<sup>63</sup> but its evolution since that time has changed its chemical composition materially. Dr. Krebs himself admits that the name was not coined until 1949, and that the name has been used since that time for the final form of the amygdalin produced by Krebs, regardless of its actual chemical composition.<sup>64</sup>

The degree of change in the composition of Krebs' amygdalin, or laetrile, over the years and the precise dates on which changes were effected, are difficult to pinpoint due to the general lack of knowledge and information on the product.

Almost without exception, the specific evidence contained in the record as to labels, clinical formulae, pamphlets relating to usage and the like do not come from the proponents of the drug who present conclusions without supporting data. Specific evidence comes from those testifying against the safety/efficacy/general recognition of laetrile who cite specific materials distributed by the laetrile proponents in support of their claims.<sup>65</sup>

<sup>63</sup> Ad.R. 184 (Affidavit of Carl M. Leventhal, M.D.) Exh. 6.

<sup>64</sup> *Id.*

<sup>65</sup> Ad.R. 434 (Affidavit of Carl M. Leventhal, M.D.) at M 280. "The testimony by laetrile proponents on use prior to October 10, 1962 do not provide information on the composition of the drug, form, strength, purity, recommended conditions of use, route and method of administration, dosage schedule."



Just as the chemical composition of laetrile has been in a state of evolution over the years, so too has its labeling with respect to the dosage to be administered and the purpose of the drug. For example, the shipment of laetrile to Dr. Cooper in 1952, which clearly was for investigational purposes,<sup>66</sup> was accompanied by a letter which addressed dosage as follows:

In these early days *it is difficult to be too specific about a good many things*, but the consensus of opinion at the moment is that the following dosage schedule is best:

For the rapid or high-grade malignancies 50mg. every other day;

For the slow or low-grade malignancies 50 to 100 mg. every five or seven days;

For the usual or intermediate case 50 mg. every three to five days.<sup>67</sup>

[Emphasis added.]

In fact, in the early 1950's uncertainty about the use of laetrile was such that in some respects Spicer-Gerhart, a manufacturer of laetrile, refrained from advising the method of use:

The injection usually is given intramuscularly although when it is possible to give it directly into the malignant lesion, this may be done with advantage. *However, perhaps one had better leave directions of that sort for a little later, after you have had some personal experience with the substance.*<sup>68</sup>

On one point, Spicer-Gerhart was quite firm: laetrile was *not* to be taken orally. According to a mimeograph prepared by the Company for guidance to doctors on the

<sup>66</sup> Ad.R. 388, Exh. 2, 3 (Affidavit of John R. Cooper, M.D.).

<sup>67</sup> *Id.*

<sup>68</sup> *Id.*, Exh. 4 (emphasis added).

use of laetrile, the substance was described as "extremely toxic by [oral] route of administration."<sup>69</sup>

In 1952 Spicer-Gerhart described the theory behind laetrile as follows:

In order that there shall be no misunderstanding, may I remind you that, according to the theory outlined, Laetrile has a destructive effect only. Certainly, this destructive effect is very definite and sometimes very quick, but it does have to be borne in mind that Laetrile makes no contribution whatever toward the remainder of the patient's problem—reconstruction and repair. From the very nature of the action of Laetrile, it will be obvious that under certain circumstances, hemorrhage might take place and mechanical problems involving the disposal of neurotic breakdown problems might arise.<sup>70</sup>

In a later pamphlet by Dr. Krebs, Sr., the following statements were made with respect to laetrile:

Laetrile does not palliate, it acts chemically to kill the cancer cell selectively without injury to the normal tissues of the body.

The usual daily dose of Laetrile is 10 mg. of the glucoside amygdalin for every pound of the patient's weight. Some patients may need 15 or even 20 mgs. but rarely more except in cases of pancreatitis enzymes insufficiency due to inhibition. . .

Laetrile is dissolved in sterile distilled water using 4 to 5 cc for every 1000 mgs. of Laetrile.

The injections should be given intravenously every day until . . .

They are not only important food for nutrition they also act as a vitamin to supply the body with the CN

<sup>69</sup> *Id.*, Exh. 5.

<sup>70</sup> *Id.*, Exh. 2.

group for the biosynthesis of another vitamin cyanocobalamine.<sup>71</sup>

The record abounds with other examples of labeling changes with respect to laetrile. For instance, the affidavit and supporting exhibits submitted by Robert S. K. Young, Ph.D., compared the labeling and other information contained in the New Drug Application for laetrile (NDA 14-032) received by the FDA during an establishment inspection of Krebs Laboratories on April 23, 1965. Dr. Young identified some of the significant labeling differences as follows:

(a) The formulation of the drug had been changed. In 1962, the formulation contained N, N diisopropylammonium iodide and saccharides in addition to amygdalin and these materials were to be reconstituted with an isotonic solution. In 1965, the formulation contained only amygdalin and this material was to be reconstituted with water, which is not isotonic.

(b) The class of patients for whom the drug is recommended had been changed. In 1962, the label characterizes the drug as a palliative agent for use in "cancers beyond aid by standard agents," and warns that "*It is not to be employed to the exclusion of surgery, radiation or similar standard modalities so long as they are indicated.*" The 1965 labeling states that "Laetrile does not appliate, it acts chemically to kill the cancer cell selectively without injury to the normal tissues of the body." It goes on to warn that "The physician who is using laetrile to palliate his patients is not doing justice to his patient."

(c) The interaction of Laetrile with other forms of cancer treatment had been changed. In 1962, the

<sup>71</sup> Ad.R. (Affidavit of Robert S.K. Young, M.D., Exhibit C) which includes labeling obtained during an April 23, 1965 inspection of the Krebs Laboratories in San Francisco.

label states Laetrile "has no known therapeutic incompatibilities." It goes on to warn that "the general enhancement of the clinical condition of the patient is not to be considered as justification for the exclusion of standard modalities so long as they are applicable." In the 1965 material, the directions state that "The less drugs and medicines given, during the Laetrile treatment, the better. What should be especially avoided is . . . other cancer therapies, strong drugs . . . etc."

(d) The recommended route of administration had changed. In the 1962 labeling, "intravenous administration is preferred." The 1965 labeling advises that "Whenever it's possible to administer Laetrile by injection into the artery supplying the involved area this administration should be used." Specifically, injection into the external carotid or its branches, abdominal aorta, or internal iliac arteries is recommended. The 1965 labeling also recommends injection into the vault of the vagina and scrotal sac, and rectal enemas. I am generally familiar with the literature and reports relating to Laetrile and am aware that since 1965, there has been commercial distribution of dosage forms of Laetrile including tablets containing amygdalin, capsules of ground defatted apricot kernels, and a milkshake mix containing amygdalin all intended for oral use.

(e) The claimed mechanism of action of the drug had changed. In the 1962 material, the "Beardian thesis" was discussed as a theory. The 1962 labeling made no claim that Laetrile is a vitamin or provitamin, or that cancer is a deficiency disease. The 1965 labeling states that "Cancer is a deficiency disease" and there is a presentation of what role amygdalin plays in the therapy of cancer in light of cancer of deficiency disease.

11. All of the above changes are medically important or have medically important implications that must

be reviewed scientifically. In the same order as I have reviewed them in 10, they are:

a. Formulation changes may reflect changes in the drug substance, and always reflect changes in the material to be administered.

Whenever the material to be administered is changed, it is important that the new material be essentially identical to the old material in strength, quality and purity.

b. The 1962 labeling restricts the use of Laetrile to those patients who all have conventional therapy, and prescribes use for the purpose of palliation of their disease. The 1965 labeling states that this drug should be used to mitigate the effects of the disease and implies that the drug is of curative value. Since Laetrile has no demonstrable effect on cancer, to use Laetrile in lieu of conventional therapy is to condemn to certain death those patients with curable forms of cancer, and to prolong the pain and suffering of those patients with treatable forms of cancer.

c. The 1962 mailing label warns that the conventional therapy not be withheld during Laetrile administration. The 1965 labeling suggest conventional therapy. Again, since Laetrile has no demonstrable effect on cancer, to use Laetrile in lieu of conventional therapy is to condemn to certain death those patients with curable forms of cancer and to prolong the pain and suffering of those patients with treatable forms of cancer.

d. Changes in the route of administration of a drug must always be scientifically validated. A drug may not be effective or may be more toxic when given by different routes of administration. The recommendation in 1965 that the drug be given by intra-arterial injection is particularly hazardous. These high pressure blood vessels

are difficult to enter successfully and are prone to continued bleeding after entry with a needle.

e. The claimed mechanism of action strongly suggest that Laetrile has a rational basis as a cancer therapy. Since it has no demonstrable value as a cancer therapy, to suggest that it has may influence some to use it who might not otherwise use it.<sup>72</sup>

Dr. Young's conclusion regarding "the numerous changes which have occurred in the composition, labeling, routes of administration, dosage form, intended uses and identity" of laetrile between 1962 and 1965<sup>73</sup> in and of itself precludes laetrile from entitlement to the grandfather exemption contained in Section 107(c) (4).<sup>74</sup>

Ernest Krebs, Jr. at the hearings in Missouri stated that the dosage recommended for amygdalin has grown from 50 milligrams in 1932 to 17,000 milligrams today.<sup>75</sup> The book "World Without Cancer" discredits the 1953 California report of the analysis of patients treated with laetrile on the basis that the dosage given them was too low, only one fifteenth of the dose used now.<sup>76</sup>

Dr. Carl Leventhal sets forth an apt illustration of the importance of consistency in drug formulation and content:

Production of drugs may in a rough sense be analogized to baking a cake. Two cooks may start with identical ingredients, but the results of their labors may have different characteristics even if the same

<sup>72</sup> Ad.R. 201 (Affidavit of Robert S.K. Young, Ph.D.) at 2.

<sup>73</sup> *Id.* at 2.

<sup>74</sup> Pub. L. 87-781, reprinted at 21 U.S.C.A. § 321 note and in Appendix B hereto.

<sup>75</sup> Ad.Tr. 238 (Testimony of Ernest Krebs, Jr.).

<sup>76</sup> Tr. 333.



recipe is used. In the case of drugs, slight and frequently unnoticed deviations in processing result in the production of essentially different drugs. This is particularly true in the case of amygdalin, since, during the manufacturing process, if ground, moist kernels are, prior to dilution, allowed to stand for a period of time, such as overnight, any amygdalin presented in the material can be transformed into cyanide, benzaldehyde, and sugar by enzymatic action. In such an instance there would be a diminished amount of or no amygdalin in the finished product."

Ad.R. 434 at M 279

It is manifest that both the composition of laetrile and the manufacturer's claims with respect to its use have changed dramatically over the years. Accordingly, laetrile does not meet the continuity-of-labeling requirements of the 1962 grandfather exemption and thus is not excused from the "new drug" requirement of the Food and Drug Act.

**3. *Laetrile Is Not Entitled To Grandfather Status Because It Was Not Used or Sold Commercially Within the United States Prior to October 9, 1962***

Although the record contains evidence of use by physicians and others of a substance called laetrile prior to October 10, 1962, this limited use fails to constitute commercial use or sale as required by the grandfather provisions of the 1962 amendments. The requirements of commercial use or sale within the United States set forth in qualification (A) of the 1962 grandfather clause<sup>77</sup> means that the item must have been openly and readily available in the ordinary course of business as well as

<sup>77</sup> Section 107(c)(4), Pub. L. 87-781, reprinted at 21 U.S.C. § 321 noted in the statutory appendix.

free of all restrictions placed on investigational use.<sup>78</sup> Laetrile fails to meet either of these criteria.

First, laetrile certainly has not been openly and readily available in the ordinary course of business. The only record evidence of laetrile's marketing concerns limited and isolated manufacturing and distribution in the United States and some use outside of the United States. Use outside of the United States is not relevant to the grandfather exemptions in that the law specifically limits applicability to substances sold in the United States. Second, laetrile sales that did take place within the United States were neither widespread nor unqualified.

According to the developer of laetrile, the use of the drug in the U.S. was clearly for investigational purposes only. In an affidavit executed by Dr. Krebs, Sr. in 1965 he claimed:

7. As early as 1926 and up through 1962, I first began to ship and have done so continuously thereafter the Scarcarcinase extract (cf2), first the amygdalin (cf3), then the purified amygdalin (cf4), then the purified and lyophilized amygdalin (5), and then since 1949 (cf6) the latter under the name *Laetrile* to persons in other States outside of the State of California and in many other countries. *The above shipments were for investigational use only.*<sup>79</sup>

In fact, the record demonstrates that the manufacturers of laetrile held it forth for investigational use only as late as 1970. In 1962, an application for a new drug application (NDA) was submitted to the FDA for its consideration and in 1970 an application of an In-

<sup>78</sup> *Durovic v. Richardson*, 479 F.2d 242, 247-48 (7th Cir. 1973), cert. denied, 414 U.S. 944.

<sup>79</sup> Ad.R. 183 (Affidavit of W. Sherwood Lawrence, M.D.), Attach. 6, at 2 (emphasis added).

vestigational New Drug (IND) also was submitted.<sup>80</sup> These actions are significant because it has been judicially recognized that the presentation of an IND or NDA to the FDA implies that on those dates the drug involved was a "new drug"; otherwise the NDA or IND would not be required.<sup>81</sup>

Thus, the proponents of laetrile by their own actions have characterized laetrile as "new" and "investigational," and hence not "commercial" within the meaning of the 1962 transitional provisions. Consequently, laetrile is not entitled to a grandfather exemption.

Finally, the commercial availability of the chemical amygdalin from drug supply houses cannot provide a buttress for the district courts finding that laetrile was commercially marketed prior to October 9, 1962 (Pet. App. at pp. 29a-30a note 21). As Dr. Carl Leventhal made clear on the record in the rulemaking proceeding, the commercial availability of a chemical used for drug formulation purposes "does not establish protection under a grandfather clause for a finished dosage form of that chemical when it is labeled and offered for drug use."<sup>82</sup> Dr. Leventhal illustrates as follows:

In this regard amygdalin is no different from any other chemicals and botanical substances from which newer preparations are derived. For instance, rauwolfia serpentina, a climbing shrub, contains in its root, reserpine, and has been used for centuries for medicinal purposes. However, when reserpine was extracted from rauwolfia reserpine, processed into a finished dosage form, and labeled for particular

<sup>80</sup> See *Id.*, Ad.R. 184, Ad.R. 434, Ad.R. 201, and Ad.R. 431, (Affidavits of W. Sherwood Lawrence, M.D., Carl M. Leventhal, M.D., Robert S.K. Young, M.D., Bryant L. Jones).

<sup>81</sup> *Durovic v. Richardson*, 479 F.2d 247 (7th Cir. 1973), cert. denied, 414 U.S. 944.

<sup>82</sup> Ad.R. 434 at M 278.

therapeutic uses, it was and is considered to be a new entity. The same is true of Laetrile or Vitamin B-17 for these drugs are different in not only their composition and dosage form, but bear labeling claims which were not associated with the ancient botanical sources.<sup>83</sup>

The ingredients used to manufacture the alleged cancer drug may have been available commercially but the commercially available substances were not sold as treatment for cancer.<sup>84</sup> It is the product produced from the various

<sup>83</sup> *Id.* at page M 278-79; see Ad.R. 416 at M 70-71.

<sup>84</sup> Ad.R. 434 at M 278-79; Ad.R. 416 at M 70-71.

The commercially available chemical compounds referred by Dr. Burk, the bitter almond listed on the "GRAS" list (Generally Regarded As Safe) of the FDA, is an oil used for flavoring and contains no amygdalin. It is not as suggested by Dr. Burk, laetrile Affidavit Exhibits I and J. Further, the oil of bitter almond compound referred to in the Merck Index is not the compound suggested for cancer treatment by Mr. Krebs. And the references to its use in Egypt or Russia for malignancies is pure and unsubstantiated hearsay. Ad.R. 434, Ad.R. 435. (Testimony of Richard H. Lange, M.D.) Indeed, the use in Russia was of a sweet almond mixture thought to be a narcotic. Ad.R. 434 at M 278. The claim made by the laetrile proponents in the FDA proceedings that the drug is grandfathered because it was contained in the Merck Index or used by the ancient Egyptians were in substantial part presented for court decision in *Hanson v. United States*, 417 F. Supp. 30, 36 (D. Minn. 1976). Unpersuaded, the court stated:

The only evidence presented by the plaintiffs to try to establish that their tablets and vials of laetrile are exempt under the "grandfather" clause of § 321(p)(1) consists of the 1896 edition of Merck's Index and hearsay concerning the use of amygdalin during historical times dating back to the ancient Egyptians. This evidence is patently insufficient to demonstrate that the exemption applies. Merck's Index contains no information about the intended use of amygdalin, providing only certain facts as to its physical appearance, melting point, and source. The only reference to the conditions of its use is the phrase "Keep well stoppered." There is no indication therein that amygdalin in tablet form or in liquid form was in use for any purpose whatsoever; there is certainly no indication that amygdalin liquid was being injected intravenously into human beings or that amygdalin tablets were being ingested

available chemical compounds that is the allegedly cancer active agent to be evaluated, not the independent chemical ingredients.

***4. Laetrile Is Not Entitled To A Grandfather Exemption Under The 1962 Drug Act Amendments Because The Drug Has Never Been Generally Recognized As Safe For The Treatment Of Cancer Either In Terms Of Toxicity Or Effectiveness***

a. *The general recognition standard.* The elements required for general recognition of safety are correctly stated by the Commissioner in his decision at Pet. App. 155a:

... for a drug to be generally recognized as safe it must have accumulated at least the amount of evidence and safety that would be required for the approval of a new drug application and that evidence must be generally available to the community of experts through publication in the scientific literature. In order for a new drug application for a drug to be approved, there must exist as to that drug "adequate tests by all methods reasonably applicable" that show the drug's safety (21 U.S.C. 355(d); cf. 21 CFR 314.111(a)(1))

The Commissioner's criteria tracks this Court's decision in the *Hynson* case. This Court in *Hynson* conceded that while Section 201(p) of the Act was both "quantitative and qualitative", on its face it failed to offer definitive guidance to the FDA with respect to its enforcement because a definition of what constitutes "general recognition" among experts was not to be found in the Act.

by human beings. In short, there has been no showing by the plaintiffs that laetrile tablets or liquid were "subject to" the Act prior to the enactment of § 321(p)(1), and no showing that "at such time its labeling contained the same representations concerning the conditions of its use."

Consequently, this Court looked to the overall statutory scheme of the Act and the overriding purpose of the 1962 Amendments and then articulated the standard to be applied, namely, that general recognition by experts presupposes an expert consensus founded upon substantial evidence as defined in Section 505(d) of the Act. 412 U.S. at 632. The elements of substantial evidence as set forth in that Section of the Act consists of adequate and well-controlled investigations, including clinical investigations by experts qualified by scientific training and experience to evaluate the drug involved, in this case for safety. The quality of these investigations should be such that the experts can conclude from them whether the drug will, in this case, be safe under the conditions of use prescribed, recommended or suggested in the labeling or proposed labeling. The scientific evaluation criteria articulated by this Court affords to the consumer the protections envisioned by then President Kennedy when he recommended the strengthening of the federal drug laws. "The physician and consumer should have the assurance, from an impartial scientific source, that any drug or therapeutic device on the market today is safe and effective for its use; that it has the strength and quality represented; and that the accompanying promotional material tells the full story—its bad effects as well as its good." (1962) U.S. Code Cong. & Admin. News, 4143-4144.<sup>88</sup>

<sup>88</sup> See also *Pharmaceutical Manufacturers Ass'n v. Richardson*, 318 F. Supp. 301, 307 (D. Del. 1970), in which the court cited witnesses before the hearings leading to the 1962 Drug Amendments corroborating President Kennedy's call for impartial judgments on drugs: "(A) collection of impressions will (not) furnish the truth . . . (T)his approach did not prevent doctors from having unbound faith in the curative powers of leeches for hundreds of years before scientific evaluation became the preferred means of judging efficacy of therapy . . . (The) magnitude of sales of a drug after vigorous promotion is no recommendation for its usefulness or efficacy . . ."

[Footnote continued on page 58]



The district court pays lip service to the general recognition criteria but its application of that criteria falls short. The district court relies not on the scientific consensus reflected in the record as a whole, from experts qualified by scientific credentials and recognition of their status by their peers, but rather on selective anecdotal experiences and submissions of laetrile proponents which are not supported by the objective scientific testing and respected publication criteria which are required by this

<sup>85</sup> [Continued]

See also, the opinion of Judge Smith in *United States v. Articles of Food and Drug*, 372 F. Supp. 915, 920-921 (N.D. Ga. 1974):

Quite properly, it is simply not enough to show that some people, even experts, have a belief in safety and effectiveness. *A reasonable number of Americans will sincerely attest to the worth of almost any product or even idea. To remove the aberrations in uniformity which can result from a well-staged "swearing match," the law requires more.* Indeed, it has been heretofore held that the purpose of the normal inquiry is not to determine safety and effectiveness at all, but to ascertain the drug's general reputation in the scientific community for such characteristics. *United States v. 41 Cases, More or Less*, 420 F.2d 1126 (5th Cir. 1970); *AMP, Inc. v. Gardner*, 389 F.2d 825 (2nd Cir. 1968), cert. den., 393 U.S. 825, 89 S.Ct. 86, 21 L.Ed.2d 95 (1968). It is certain that a conflicting reputation is insufficient to establish general recognition. *United States v. An Article of Drug—Furestrol Vaginal Suppositories*, 294 F.Supp. 1307 (N.D. Ga. 1968), aff'd 415 F.2d 390 (5th Cir. 1969).

Therefore, what is required is more than belief, even by an expert; it is a general recognition based upon substantial scientific evidence as delineated in the regulatory guidelines. 21 CFR § 130.12. *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609, 619, 93 St. Ct. 2469, 37 L.Ed.2d 207 (1973). There is no reason to differentiate the holding in *Hynson* between human drugs, and animal drugs. *United States v. 14 Cases—Naremeo Medimate*, 374 F.Supp. 922 (W.D. Mo., Number 2806, January 29, 1974). Public health considerations are similar. Further, logic would dictate no lesser standard after-the-fact than in securing an application. Indeed, the reasoning of the Supreme Court appears to be that "the reach of scientific inquiry" is the same whatever the forum. *Weinberger v. Bantex Pharmaceuticals, Inc.*, 412 U.S. 645(b), 93 S.Ct. 2488, 37 L.Ed. 2d 235 (1973). [Emphasis added; footnote omitted.]

Court. In contrast, in arriving at his decision that there is no general recognition of the safety of laetrile, the Commissioner, as detailed below, scrutinized the record as a whole and evaluated the evidence quantitatively and qualitatively by application of the standards obtained in the statute as interpreted by this Court.

b. *The safety standard.* Where life-threatening illnesses such as cancers are involved, satisfaction of the safety standard of the grandfather clause must include a showing that the drug is both effective and non-toxic. The effectiveness requirement is discussed at pp. 15-18, *supra*. Briefly, at the hearings on the 1962 drug amendments, Secretary Ribicoff informed the Committee considering the bill that where progressive of life-threatening diseases such as cancer were involved, the administrative agency already required a showing of effectiveness as well as drug safety. The Senate report on the bill establishes that this administrative practice was expressly preserved vis a vis the new drug amendments: "The provisions of the bill are in no way intended to affect any existing authority . . . to consider and evaluate the effectiveness of a new drug in the context of passing upon its safety" (1962) U.S. Code Cong. & Admin. News at 2892. If effectiveness, as found by the district court as a matter of law (Pet. App. at page 28, note 18) could not be considered by the Commissioner in passing upon the "safety" of a drug intended for cancer, the Commissioner's pre-existing authority would certainly be "affected". His authority would be diminished. The language of the Committee interpreting the reach of the proposed legislation permits no such result.

Further, the requirement that drugs used in treatment of life-threatening diseases be effective in order to meet the "safety" standards of the 1962 grandfather exemption was squarely addressed in the *Durovic* decision. After recounting the administrative interpretation ac-

corded by the FDA to the safety requirement and after reviewing pertinent legislative history, the Court of Appeals in *Durovic* concluded:

Bearing in mind the weight properly accorded to administrative construction, and Congressional awareness of the administrative view that the concept of safety in the law before the 1962 amendments included the concept of effectiveness for its indicated use where the drug is offered for use in the treatment of life-threatening disease, we think the definition of new drug before the amendments should be construed accordingly. It would follow that a drug offered for use in the treatment of cancer is now, and was before the amendments, a new drug unless it has achieved general recognition among the experts as safe and effective for such use.

Under that analysis, the status of a drug offered for such use would be subjected to the same test before and after the amendments, and the grandfather clause would have no effect on it.<sup>86</sup>

The record in the rulemaking proceeding supports the Commissioner's decision that there exists an overwhelming consensus among qualified experts that laetrile was not generally recognized as safe in terms of effective for the treatment of cancer on October 9, 1962. Typical of the views of qualified experts toward laetrile is that of David T. Carr, M.D., a Professor of Medicine at the Mayo Medical School with wide experience in the cancer field. According to Dr. Carr:

I am informed and understand that amygdalin is a cyanogenic glycoside. Cyanogenic glycosides are chemicals which contain in their molecular structure a sugar, a non-sugar, and the cyanide group, ( $-C \equiv N$ ). I know of no cyanogenic glycoside that is generally recognized as safe and effective for the pre-

<sup>86</sup> 479 F.2d at 250 (footnotes omitted).

vention, treatment or cure of cancer, for the relief of pain associated with cancer, or for any medical purpose. The composition of the cyanogenic glycosides, in general, and of amygdalin, in particular, is such that I do not recognize them, and they are not generally recognized among experts qualified through scientific training and experience to evaluate drugs, as safe and effective for the treatment of cancer, for prophylaxis against cancer, for relief of pain associated with cancer, or for any medical use. Neither amygdalin nor any other cyanogenic glycoside was generally recognized as safe for any such uses on October 19, 1962. None of these substances has ever been so recognized. The scientific literature contains no reports of adequate, well-controlled, scientific studies, or other evidence upon which such recognition may be predicated. I know of no recognized medical test in which use of amygdalin or any cyanogenic glycoside is recommended. I know of no medical school where use of these substances is taught. I know of no expert in cancer chemotherapy who is of the view that there is evidence these substances have any useful effect in treating cancer. I know of no report in the scientific literature describing an adequate, well-controlled study which demonstrates that amygdalin or any cyanogenic glycoside is safe and effective. Furthermore, I know of no cancer expert who would want a member of his family or himself to be treated with amygdalin if cancer should develop.<sup>87</sup>

<sup>87</sup> Ad.R. 176 at 4E, see also affidavits of: Robert C. Eyerly, M.D. (Ad.R. 167); George J. Hill, II, M.D. (Ad.R. 17); David T. Carr, M.D. (Ad.R. 176); John T.P. Cudmore, M.D. (Ad.R. 178); Bernard T. Korbitz, M.D. (Ad.R. 181); W. Sherwood Lawrence, M.D. (Ad.R. 183); Carl M. Leventhal, M.D. (Ad.R. 184); Daniel S. Martin, M.D. (Ad.R. 185); Joseph F. Ross, M.D. (AF-21 at 6-8); Philip S. Schein, M.D. (Ad.R. 191); Michael B. Shimkin, M.D. (Ad.R. 192); Jesse L. Steinfeld, M.D. (Ad.R. 194); C. Chester Stock, Ph.D. (Ad.R. 195); Alfred Suffer, M.D. (Ad.R. 266); Susan J. Mellette, M.D. (Ad.R. 420).

As noted above, it is considered particularly significant by the courts in determining the presence or absence of general recognition by experts as to safety whether adequate and well-controlled investigations of the drug have been accomplished and whether there is present a body of credible literature affirming safety.<sup>88</sup> The record in this case is devoid of evidence establishing that such investigations as toxicity/efficacy have been accomplished. To the contrary, the record abounds with sworn testimony by specialists well acquainted with the relevant literature and the state of expert opinion concerning cancer research, who declare without exception that no recognized expert in the field of cancer believes now or has ever believed that laetrile is safe or effective for the treatment of that disease. In the opinion of many experts, laetrile is highly toxic when taken orally.<sup>89</sup> Other experts note that there is a lack of evidence establishing that laetrile is non-toxic when taken parentally. According to the affidavit of Thomas H. Jukes, Ph.D.:

Most items used as foods are not safe for injection, and amygdalin under the name, "laetrile", is frequently injected into cancer patients, apparently without immediate toxic effects. The toxic effects of injecting foreign substances may not show up for months or years. To be safe for injectable purposes, a compound must be shown by means of long-term toxicity tests not to produce pathological changes. No such data are available for amygdalin. (Ad.R. 416 at 1756.)

In this respect, it must be kept in mind that the grandfather exemption requires a positive showing that

<sup>88</sup> U.S. v. 1,048,000 Capsules More or Less, 347 F. Supp. 768, 771 (S.D. Tex. 1972).

<sup>89</sup> See e.g., Affidavits of Joseph F. Ross, M.D., Ad.R. 190, Chester Stock, Ph.D., Ad.R. 195, Donald C.S. Tan, M.D., Ad.R. 197, Exhibit 5. And see the chart on general recognition of safety at pp. 69-71, *infra*.

a drug had been generally recognized by qualified experts as non-toxic. There is no "presumption" of such general recognition; it is not necessary to affirmatively demonstrate toxicity. Rather, the burden of proof remains on those who seek to invoke the grandfather exemption. Such an affirmative showing is absent from this record. Additionally, where there has been little testing of a drug or where there is a dearth of medical literature on the question of its toxicity, the drug cannot possibly meet the grandfather requirements of general recognition among qualified experts. *United States v. 41 Cases, More or Less*, 420 F.2d 1126 (5th Cir. 1970). See discussion at pp. 56-59, *supra*.

Finally, a recent Massachusetts court order in a case involving a minor treated with laetrile and a coroner's report of a laetrile patient death attributed to acute cyanide poisoning both support the emerging profile of laetrile as a toxic and dangerous substance.

In the case involving the child<sup>90</sup> Judge Guy Volterra by Interlocutory Order of January 22, 1979, after finding that the child's parents were giving him laetrile which "is dangerous to health", directed the parents to submit the minor to urine thiocyanate and serum thiocyanate tests to monitor whether the child is at risk of chronic cyanide poisoning.<sup>91</sup> After receiving the report of the physician, by order of January 31, 1979, Judge Volterra found that the child indeed was suffering from chronic cyanide poisoning stemming from laetrile therapy: "The Court has accepted into evidence today a new laboratory test which indicates a level of free cyanide in the child's blood at twice the normal level."<sup>92</sup>

<sup>90</sup> Custody of a Minor, Superior Court Civil Docket No. 78-6815, Commonwealth of Mass., Plymouth Division, The Courts orders of January 22, 1979 and January 31, 1979 are appended hereto as Appendix C.

<sup>91</sup> *Id.*

<sup>92</sup> *Id.*



The Coroner of Alameda County, California, in a report attached as Appendix B, determined that a female cancer patient who was receiving laetrile treatment died of cyanide intoxication. The cyanide levels in her blood were 3/8 mcg/ml. The deceased's laetrile treatment commenced in March of 1978 with a dosage of 9 grms every day for 30 days, then reduced to 3 grms thrice weekly, later reduced to twice weekly and she was on the last course of treatment (once a week injections) when she died. If the deceased was unable to come in for injections, her instructions were to take 1000 mgm tablet of laetrile.

As graphically demonstrated on Tables A and B which follow, laetrile has not satisfied the general recognition criteria for safety either in terms of toxicity or effectiveness, neither has it shown consistency in formulation, purity, mechanism of action, labeling, claims, dosages, or method of administration, all of which are required to gain a grandfather exception. The record supports the Commissioner's denial of such an exception and the error of the district court in granting an exemption.

# REQUIREMENTS FOR THE 1962 GRANDFATHER CLAUSE

Dates	Mechanism (Rationale) of Drug Action	Label/Pamphlet claims for Laetrile	Formulation	Method of preparation (Reconstitution)	Dosage	Route (Method of) Administration	Use As An Investigational Drug/Not Commercially Marketed	Laetrile Label & Pamphlets—Representation Safety/toxicity
1920's			apricot extract containing "emulsin", "amygdalase", "prunase", "Pectinase" (1)			IV-single injection process (8)		
1926			apricot extract called "sarcarcinase" which was amygdalin + 1 glucosidase (2)					
1929			"sarcarcinase" is less than 5% amygdalin (3)					toxic-IV (6)
1932			apricot extract rich in glucosidase & amygdalin (4)					
1936			amygdalin purity is 66% (7)					
1932			amygdalin minus emulsin (11)	isotonic solution (28)	50mg every 3-5 days (16) 20mg (17)	IV of cyanogenic glucoside in 5 minutes by IV of the enzyme Beta-glucosidase (9)	Investigational use (12) Krebs foundation set up in 1963 "to foster the investigation of Laetrile." (13)	not for oral administration (15)
1932			prunasin biosynthesized (21)			IM injection of Laetrile ff. by Beta-glucosidase (23)	Laetrile first tried in humans in June of 1962 (14)	
1932			amygdalin lyophilized (22)			IM injection (23) tamponade (23) lontophoresis (23)		extremely toxic orally (20)
1952-1955			prunasin—amygdalin with one molecule of glucose instead of two (25)					
1958			1-mandelo nitrile-beta-glucuronic acid (26)					
1959			amygdalin purity is 99.8% (35)					
1959		reduces size of malignant tumor (71)						
1960								
1961								
1962	Beardian thesis (29)	palliative agent not for oral administration (30)	N,N diisopropylammonium iodide and saccharides in addition to amygdalin (33)	isotonic solution (36)	1000mg (28) 1-2 grams every day (37) 3,000-5,000mg. (38)	IV or IM injection (40)	All amygdalin compounds used from 1926-1962 were shipped for "Investigational use only" (41)	not to be taken orally, it is extremely toxic by that route of administration (42) "Laetrile is relatively non-toxic when administered parenterally." "Orally it is extremely toxic due to the release of hydrogen cyanide on contact with the hydrochloric of the gastric juices." (43)
1962	Krebs cyanide theory (72)	not to be employed to the exclusion of other cancer treatment modalities (31) applicable to carcinomas, sarcomas, Hodgkins disease (32) not recommended for the leukemias (32)	Of 4 identically labeled Laetrile samples, 2 contained iodine as an additive and 2 did not (34)		10-20mg. of the glucoside amygdalin for every lb. of patient's weight, daily (39)			
1963								
1965	Cancer is a deficiency disease and Laetrile is a vitamin for that deficiency (46)	kills the cancer cell (47) Avoid other cancer therapies; only take Laetrile (48)	preparation only contained amygdalin (49) preparation contained 87-98% amygdalin with varying amounts of sucrose, phenol and diisopropyl ammonium iodide (50) US/Canada product labels same: A-B-Cyanogenic glucoside; US contained 87 + 2% amygdalin; Canada -98 + 2% amygdalin; US also contained phenol, iodide, sucrose; the different formulation reflected in "marked biochemical difference" in testing. (51) amygdalin contained not less than 96% of C20H2NO (55) Amygdalin MF (56)	water (52)	10-15 mgs per lb. patient weight (53) 20mgs. per lb. body weight (53)	oral (44) Interarterial enemas oral (54)		Krebs Laboratories offers oral Laetrile and states that it is non-toxic (45)
1969	Passwater's cellular oxidation and fermentation process (72)				size/frequency of dosage has not been precisely determined (57) 3-6grms/70kg every 24 hrs (57) 3-6grms/day (59) 800mg./day (62)		"amygdalin is still an investigational drug" (58)	
1970						IV injection not orally (60) oral capsules (63)	Investigational drug (61)	Laetrile capsules: oral use-non toxic cyanide glucoside (64)
1971								
1976				Unreliability of formulation (65)				
1977	Brehman & Dardymor's adaptogenic glycosides stimulating the production of immune bodies (72)	prevent, control cancer, pain relief, appetite increase, weight gain, feeling of well being (66) Laetrile is not a cancer cure, it may effect control (66)b	formula variability of 14 to 87% amygdalin in injection solutions formula variability of 42-450 mg. amygdalin per 500 mg. tablet in oral medication (67)a		6-9 grams/day (67)b 17000milligrams (68)	IV injection supplemented by oral tablets (69)		
1978			Laetrile chemical formula: C14H15NO7 (73) Amygdalin chemical formula: C20H27N11 (73)		9 grams (day) reduced to 3 grams (twice weekly) reduced to 2 grams (bi-weekly or 1000mgm orally (70)	IV oral (70)		

## REFERENCES FOR TABLE A

- (1) Ad. R. 260 at p. 1-2
- (2) Ad. R. 167 Attch. 13
- (3) Ad. R. TS26
- (4) Ad. R. 183 Attch. 7 at p. 23
- (5) Ibid.
- (6) Ad. Tr. 238
- (7) Ad. R. 183 Attch. 13¶ Ad. R. 184 at p. 9 and Exh. 6
- (8) Ad. R. 184 Exh. 6 at p. 2
- (9) Ad. R. 183 Attch. 7 at p. 24
- (10) Ad. R. 388 Exh. Nos. 2, 4
- (11) Ad. R. 183 Attch. 7 at pp. 23-26
- (12) Ad. R. 388 Exh. 2
- (13) Ad. R. 184 Exh. 5 at p. 3.
- (14) Ad. R. 184 at p. 9 & Exh. 5
- (15) Ad. R. 184 Exh. 5 at p. 3.
- (16) Ad. R. 167 Exh. 2
- (17) Ad. R. 183 Attch. 6
- (18) Ad. R. 388 Exh. Nos. 3, 4
- (19) Ad. R. 388 Exh. 4
- (20) Ad. R. 388 Exh. Nos. 4, 5
- (21) Ad. R. 183 Attch. 7 at p. 26
- (22) Ad. R. 183 Attch. 13
- (23) Ad. R. 183 Attch. 7 at pp. 26-31; Ad. R. 184 at p. 9
- (24) Ad. R. 388 Exh. 4 at pp. 6-7
- (25) Ad. R. 183 Attch. 7 at p. 26
- (26) Ad. R. 183 Attch. 7
- (27) Ad. R. 167 Exh. 2
- (28) Ad. R. 183 Attch. Nos. 6 & 16 at p. 22
- (29) Ad. R. 201 at H234; Dorr, Paximos "The Current Status of Laetrile" 89 *Annals Of Internal Medicine* 390-391 (1978)
- (30) Ad. R. 201 at H.232 & Attch. 1
- (31) Ad. R. 201 at H.232
- (32) Ad. R. 201 Attch 1
- (33) Ad. R. 201 at H.232; Ad. R. 183 Attch. Nos. 17, 16 at p. 21.
- (34) Ad. R. 183 Attch. 16 at pp. 27-28
- (35) Ad. R. 183 Attch. 13; Ad. R. 184 at p. 9 and Exh. 6
- (36) Ad. R. 201 at H.232
- (37) Ad. R. 201 Exh. B at 104
- (38) Ad. R. 167 Exh. 2
- (39) Ad. R. 183 at p. 4 & Attch 8 at p. 3.
- (40) Ad. R. 201 at H.233
- (41) Ad. R. 167 Attch. 3
- (42) Ad. R. 183 at p. 16
- (43) Morrone, John A., M.D., "Chemotherapy Of Inoperable Cancer; A Preliminary report of 10 Cases Treated With Laetrile, 20 *Journal of Experimental Medical Surgery* 299-308 (1962)
- (44) Ad. R. 183 Attch. 4C
- (45) Ad. R. 183 Attch. 4C
- (46) Ad. R. 201 at H.234; *Annals* supra note 29 at p. 391
- (47) Ad. R. 201 at H.232 and Exhb. C
- (48) Ad. R. 201 at H.233
- (49) Ad. R. 201 at H.232
- (50) *Annals*, supra note 29 at p. 389-390
- (51) Ad. R. CO251 Attch. 14 "Supplementary Report by the Cancer Advisory Council on the treatment of cancer with Beta-cyanogenetic Glucosides" Part III, Study of Its Physiochemical and Biochemical Properties, Table 1 at 22 and at pp. 19-26. See also 92 *Canadian Med. Assoc. Journal* 1057-1061 (May 16, 1965)
- (52) Ad. R. 201 at H.232 and Exh. C
- (53) Ad. R. 201 Exh. C
- (54) Ad. R. 201 at H.233 and Exh. C
- (55) Ad. R. 216 at 375



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|-----------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| (56) Ad. R. 174, Attch. 9                                                                                                                     | (Robert. Bradford, Committee Free Choice Cancer Therapy)                                     |
| (57) Ad. R. 216 at 384; Ct. R. 1416 at 384                                                                                                    |                                                                                              |
| (58) Ad. R. 384 at 374                                                                                                                        | (66-b) Bradford, supra, Laetrile Hearings, at p. 295                                         |
| (59) Ad. R. 183 Attch. 10                                                                                                                     |                                                                                              |
| (60) Ibid.                                                                                                                                    | (67-a) Annals, supra note 29                                                                 |
| (61) Ad. R. 184; Ad. R. 301; Ad. R. 431                                                                                                       | (67-b) Annals, supra note 29 at 395                                                          |
| (62) Ad. R. 183 Attch. 9                                                                                                                      | (68) Ad. Tr. 238                                                                             |
| (63) Ibid.                                                                                                                                    | (69) Annals, supra note 29 at 395                                                            |
| (64) Ibid.                                                                                                                                    |                                                                                              |
| (65) New England Journal of Medicine issue of November 25, 1966 at p. 1264, comment by physicians at United States Center for Disease Control | (70) Coroners Report, Appendix B hereto.                                                     |
| (66-a) Kennedy Subcommittee Laetrile Hearings, July of 1977 at pp. 246-247, 271-272 (J.A. Richardson, M.D.); pp. 295-297                      | (71) Ct. R. 1416, McNaughton Foundation Drug Brochure at 387                                 |
|                                                                                                                                               | (72) Ct. R. 1507, booklet "Amygdalin (Laetrile) Therapy" Bruce W. Halstead M.D. at pp. 25-29 |
|                                                                                                                                               | (73) Id. at pp. 4-5.                                                                         |

## TABLE B:

GRANDFATHER RIGHTS: LACK OF  
GENERAL RECOGNITION OF SAFETY/EFFICACY*Safety/Efficacy \**

Arthur I. Holleb, M.D., Sen. V.P. for Med. Affairs, ACS  
(Pet. App. 127a-128a)  
R. Lee Clark, M.D., Pres. ACS (Pet. App. 128a-129a)  
Frederick N. Silverman, M.D., Chmn. Comm. Neoplastic Diseases Am. Academy of Pediatrics (Pet. App. 129a)

\* The qualify for an exemption from new drug status, Laetrile on October 9, 1962 would have to have been generally recognized among experts qualified by scientific training and experience to evaluate the safety of drugs as safe for use under the conditions prescribed, recommended or suggested in the labeling thereof. For a drug to be recognized as safe, it must have accumulated evidence of safety through adequate tests and that evidence must be generally available to qualified experts through publication in the scientific literature (Pet. App. 155a). Bearings upon safety criteria is whether there is general recognition of Laetrile's use, formulation, conditions or use (Pet. App. 201a-204a). Further, as discussed at pp. 14-18 supra, safety in terms of life-threatening illness is by court and administrative construction prior to 1962 held to include effectiveness. This table scrutinizes general recognition of safety both as to the record on "effectiveness" as well as "toxicity". Finally, it should be noted (Pet. App. 114a) that this general recognition standard applies to adequate and well-controlled clinical (human) trials, not animal tests. However, the effects noted in animal tests reinforce the experts view on the toxicity of Laetrile. See e.g., Dorr, Paximos "The Current Status of Laetrile" 89 Annals of Internal Medicine 393-394 (1978), Lewis "Laetrile" 127 Western Journal of Medicine 55 (1977), Fenselau et al "Cancer Causing in Animals: Mandelonitrile B-Glucuronide: Synthesis and Characterization, 198 Science 625 (1977).

- William R. Barclay, M.D., American Medical Ass'n (Pet. App. 129a-131a)
- W. Sherwood Lawrence, M.D., St. of Calif. Cancer Adv. Council (Pet. App. 131a)
- Jonathan Rhoads, M.D., Chm. Presidents Nat'l Cancer Adv. Bd. (Pet. App. 131-132a)
- Jesse Steinfeld, M.D., Dean, Sch. Med., Med. College of Va. (Pet. App. 132-133a)
- Richard H. Lange, M.D., Chief, Nuclear Med., Ellis Hosp. (Pet. App. 133a-134a)
- M. Shimkin, M.D., Prof. Sch. Med., U. of Calif., San Diego (Pet. App. 134a)
- B. Korbitz, M.D., Chief, Chemotherapy Sec., Neb. Med. Hosp. (Pet. App. 134a-135a)
- Susan Mellette, M.D., Assoc. Prof. Med., Oncology, Med. Coll. of Va. (Pet. App. 135a-136a)
- D. Martin, M.D. (Pet. App. 136a-137a)
- J. Wallace, Jr., M.D., Dir. Cancer Control & Rehab., Roswell Park (Pet. App. 137a)
- J. T. P. Cudmore, M.D. (Pet. App. 137a-138a)
- Sidney Weinhouse, Prof. Biochem., Temple (Pet. App. 138a-139a)
- B. L. Jones, M.D., Med. Dir. U.S. Public Health Serv. (Pet. App. 139a-140a)
- G. J. Hill, II, M.D., Prof. Marshall Univ. (Pet. App. 140a-142a)
- V. DeVita, Jr., M.D., Director, Division of Cancer Treat., NCI (Pet. App. 142a-143a)
- R. L. Mecklenburg, M.D., Dir., Nuclear Med., Wilmington Med. Ctr. (Pet. App. 143a)
- R. C. Eyerly, M.D., Geisinger Clinic (Pet. App. 143a-144a)
- See also Pet. App. 145a-149a, 209a-211a.

#### *Safety/Toxicity*

- See Generally Pet. App. 154a-162a, 201a-206a
- W. Sherwood Lawrence, M.D., State of Calif. Cancer Adv. Council (Pet. App. 156a-158a)
- R. S. K. Young, M.D., Ph.D. (Pet. App. 158a-160a)
- Carl M. Leventhal, M.D. (Pet. App. 160a)
- J. F. Ross, M.D. (Pet. App. 162a)

#### *Ingestion of apricot pits*

- Laetrile, Apricot Pits, and Cyanide Poisoning, New England Journal of Medicine 1264 (Nov. 25, 1976)
- Cyanide Poisoning From Ingestion of Apricot Kernels—California Morbidity & Mortality, Center for Disease Control, HEW Doc. of 12/19/75
- Annals of Internal Medicine, see note below at 391.

#### *Laetrile: oral medication*

- Annals of Internal Med., see note below at p. 391.
- Smith et al "Laetrile Toxicity: A Report of Two Patients" 72 Cancer Treatment 169 (1978) (Case 2, toxicity symptoms resolved within 48 hours of discontinuing Laetrile).
- D. Maxwell, M.D., "Increased Cyanide Values In A Laetrile User" 119 CMA Journal 18 (July 8, 1978) (normal cyanide values 0.01-0.02 mg/dL; Laetrile patient experiencing toxicity levels 0.6 mg/dL; Patients who have died have cyanide levels of 0.26 to 3/1 mg/dL).
- Alameda County Coroner's Report, Appendix B hereto. Patient taking oral laetrile medication (1000 mgm tablets) died of cyanide intoxication with a blood level of 3.8 mcg/ml.

#### *Laetrile by injection*

- Annals of Internal Medicine, see note below at p. 391.
- Smith "Laetrile Toxicity" *supra*, Case 1.

### III. THE USE OF LAETRILE IN CONNECTION WITH ONE'S PERSONAL HEALTH CARE IS NOT PROTECTED BY THE CONSTITUTION

#### A. Overview

The district court in its decision found a general right to use laetrile: "By denying the right to use a nontoxic substance in connection with one's own personal health-care, FDA has offended the constitutional right of privacy" (Pet. App. 14a).<sup>93</sup> In doing so, the district court adopted the position of the laetrile proponents below that the premarketing requirements of the Act violate the cancer patient's right to privacy by inhibiting access to drugs which have not been proven safe and effective. This contention [ratified by the district court, and scrutinized here as an alternative avenue of affirmance or, as the Society submits, rejection of the court of appeals decision] raises the issue of whether the amorphous right of privacy encompasses the right to choose unsafe and ineffective drugs.

Traditionally, regulating health has been viewed as a valid and important exercise of the police power.<sup>94</sup> As such, health regulations have been upheld upon a demonstration of a rational or reasonable relationship between the statute and the purpose of the legislation.<sup>95</sup> However, should this Court decide that a patient has a fundamental

<sup>93</sup> The error of the district court in assuming that laetrile is non-toxic is discussed *supra* at pp. 59-71. The effects of permitting access to laetrile to the terminally ill on the public health and welfare are treated *supra* at pp. 23-33.

<sup>94</sup> "It is elemental that a State has broad power to establish and enforce standards of conduct within its borders relative to the health of everyone therein. It is a vital part of the State's police power." *Barsky v. Board of Regents of New York*, 347 U.S. 442 (1963).

<sup>95</sup> See *Goldblatt v. Town of Hempstead*, 369 U.S. 590, 594 (1962); *Williamson v. Lee Optical Co.*, 348 U.S. 483 (1955).

right to take a drug which has not met the safety and efficacy requirements of the Act, and thereby evoke strict judicial scrutiny, the government must justify its intrusion upon the patient's choice by demonstrating a compelling interest in the pre-marketing standard.<sup>96</sup> The American Cancer Society maintains that the safety and efficacy requirements should be judged under the rationale basis standard.<sup>97</sup> However, should this Court elect to expand "right of privacy" to include access to drugs which have not met the FDA premarketing requirements, the national interest in assuring the safety and effectiveness of a drug before it reaches the consumer and the causal nexus between the premarketing standards and the purpose of the legislation indicate that the compelling state interest standard has been met.

#### B. There Is No Absolute Right To Do With One's Body As One Chooses

As this Court noted in *Paris Adult Theatre I. v. Slayton*:

The State statute books are replete with constitutionally unchallenged laws against prostitution, suicide, voluntary self-mutilation, brutalizing "bare fist" prize fights and duels, although these crimes may only directly involve "consenting adults". Statutes making bigamy a crime surely cut into an individual's freedom to associate but few today seriously claim that such statutes violate the First Amendment or any other constitutional provision.<sup>98</sup>

<sup>96</sup> *Kramer v. Union Free School District*, 395 U.S. 621, 627 (1969), *Shapiro v. Thompson*, 394 U.S. 618, 634 (1969).

<sup>97</sup> This Court applied this standard when considering the constitutional implications of a state physician/patient identification procedure with the prescription of Schedule II drugs. *Whalen v. Roe*, 429 U.S. 589 (1977). The rational basis test was also applied when the Court considered the validity of a state statute outlawing a particular abortion procedure. *Planned Parenthood v. Danforth*, 428 U.S. 52 (1976).

<sup>98</sup> 413 U.S. 46, 68 (1973).



This Court has upheld compulsory military service,<sup>99</sup> compulsory vaccinations,<sup>100</sup> and compulsory sterilization.<sup>101</sup> Blood transfusions have been authorized despite the patient's unwillingness to consent.<sup>102</sup> Courts have universally rejected the argument that there is a constitutional right to use marijuana in the privacy of one's own home.<sup>103</sup> In an analogous area, this Court has summarily affirmed a decision rejecting claims that state legislation requiring motorcyclists to wear protective helmets violated the right to privacy.<sup>104</sup>

These cases have rejected the argument that governmental imposition of self-protective regulations is an unconstitutional invasion of a person's autonomy and right to be let alone. They collectively indicate that the government has a supportable interest in limiting personal choice to protect an individual against the possibility of self-harm. In the case of drugs, such as Laetrile, where it is substantially more difficult for the individual to make an informed and rational judgment, this governmental interest would appear to be even stronger.

#### C. Cases Cited By The District Court Do Not Adequately Support Its Conclusion That There Is A Constitutional Right To Use Laetrile

In concluding that there is a constitutional right to use drugs which have not met the FDA premarketing

<sup>99</sup> Selective Service Law Cases, 245 U.S. 366 (1918).

<sup>100</sup> Jacobson v. Massachusetts, 197 U.S. 11 (1905).

<sup>101</sup> Buck v. Bell, 274 U.S. 200 (1927).

<sup>102</sup> See e.g., Application of the President and Directors of Georgetown College, Inc., 331 F.2d 1000 (D.C. Cir. 1964).

<sup>103</sup> See U.S. v. Drotar, 416 F.2d 914 (5th Cir. 1969).

<sup>104</sup> Simon v. Sargant, 409 U.S. 1020, summarily affirming 346 F.2d 277 (D. Mass. 1972) (three judge court). See Note "Motorcycle Helmets and the Constitutionality of Self-Protective Legislation", 30 Ohio State Law Journal 359 (1969).

requirements<sup>105</sup> the district court relied primarily<sup>105a</sup> upon Justice Douglas' reference to "the freedom to care for one's health and person" in his concurring opinion in *Roe v. Wade*<sup>106</sup> and *Doe v. Bolton*.<sup>107</sup> In an apparent attempt to shape the penumbra concept he first articulated in *Griswold v. Connecticut*,<sup>108</sup> Justice Douglas indicated

<sup>105</sup> The district court found a constitutional right to use a non-toxic substance in connection with one's personal health-care (Pet. App. 41a). The assumption that Laetrile is non-toxic has been substantially refused above, however, for the purposes of this discussion, we will assume non-toxicity.

<sup>105a</sup> The district court also suggested that the opportunity to take Laetrile comes within the right "to be let alone", first articulated by Justice Brandeis in his dissenting opinion in *Olmstead v. United States*, 277 U.S. 438, 478 (1928). This suggestion overlooks the context of which Justice Brandeis initially conceived that right. In his famous dissent Justice Brandeis contended that the makers of our Constitution:

Sought to protect Americans in their beliefs, in their thoughts, their emotions, and their sensations. They confer, as against the government, the right to be let alone—the most comprehensive of rights and the right most valued by civilized men. To protect that right every unjustifiable intrusion by the government upon the privacy of the individual, whatever the means employed, must be deemed a violation of the Fourth Amendment. And the use, as evidence in a criminal proceeding of facts ascertained by such intrusion must be deemed a violation of the Fifth.

The right to be let alone is then the right of an individual to be protected from governmental surveillance, intrusion and/or disclosure of private affairs. Read in context, the "right to be let alone" has entirely different constitutional underpinnings than those at issue with the drug Laetrile. Regulation of health and health care, unlike government surveillance, intrusion or disclosure of personal matters which are specifically prohibited by the Fourth and Fifth Amendments, is not only an area in which governmental action has traditionally been accepted, it is also an area in which government action is expected.

<sup>106</sup> *Roe v. Wade*, 410 U.S. 113 (1973).

<sup>107</sup> *Doe v. Bolton*, 410 U.S. 179 (1973).

<sup>108</sup> 381 U.S. 479 (1965).

his belief that the concept of liberty includes the following rights:

(1) Control over the development and expression of one's intellect, interests, tastes and personality; (2) freedom of choice in the basic decisions of one's life respecting marriage, divorce, procreation, contraception and the education and upbringing of children; and (3) freedom to care for one's health and person, freedom from bodily restraint or compulsion, freedom to walk, stroll or lope.<sup>109</sup>

After asserting that this third group of rights are fundamental and subject to regulation only upon a showing of compelling state interest, Justice Douglas does not cite cases to the effect that freedom to care for one's health is among the fundamental rights subject to strict scrutiny under the Constitution. The discussion following the third group of rights concerns only freedom from bodily restraints, freedom of movement, and protection pursuant to the Fourth Amendment from governmental intrusion. The concept of health care is not delineated or defined by Justice Douglas. Further, Justice Douglas was not joined in his concurring opinion.

Significantly, later opinions of this Court in discussing the concept of liberty in the context of personal privacy have not subscribed in full to Justice Douglas' laundry list of fundamental rights.<sup>110</sup> In fact, only the task of protecting the familiar freedoms, which Justice Douglas recognized in his second group of freedoms, has required this Court to resort to the privacy rationale of *Roe, supra*. Specifically, Justice Rhenquist writing for the majority in *Paul v. Davis* characterized the activities the *Roe* Court found within the guarantee of personal privacy as dealing with "matters relating to marriage, procrea-

<sup>109</sup> 410 U.S. at 211-213.

<sup>110</sup> *Paul v. Davis*, 424 U.S. 693, 713 (1976).

tion, contraception, family relationships and child rearing and education. In these areas it has been held that there are limitations on the state's power to substantively regulate conduct."<sup>111</sup> Clearly, the right of privacy found in familial or social relationships differs markedly from the right that is involved when the individual desires to take a drug which may be toxic and whose efficacy has not been proved in a series of objective scientific tests.<sup>112</sup>

Furthermore, as observed by at least four commentators, recent Court decisions demonstrate a tendency to regard the right of privacy not as a penumbral product, but rather a right attendant upon the more explicit provisions of the Bill of Rights or as a right emanating from the due process clause of the Fourteenth Amendment.<sup>113</sup>

#### D. Decision To Undergo Treatment Versus The Right Of Choice Among Medical Alternatives

Illustrative of the principle that choice among medical alternatives is not at this time a decision within the zone of constitutionally protected privacy is this Court's holding in *Planned Parenthood v. Danforth*.<sup>114</sup> There, this Court struck down a state prohibition of a particular abortion procedure, saline amniocentesis.<sup>115</sup> However, the Court did not hold that the prohibition violated any right to privacy. It did not hold that, because the right of privacy encompasses a woman's decision to have an

<sup>111</sup> *Id.*

<sup>112</sup> See *supra* at pp. 56-59.

<sup>113</sup> Levy, Martin R. and Hectus, C. Thomas, "Privacy Revisited: The Downfall of Griswold", 12 University of Richmond Law Review 627 (1978); Hayman, Phillip B. and Barzelay, Douglas E. "The Forest and the Trees: *Roe v. Wade* and Its Critics", 53 Boston University Law Review 765 (1973).

<sup>114</sup> 428 U.S. 52 (1976).

<sup>115</sup> *Id.* at 79.

abortion, the state may not prohibit a particular abortion procedure. Rather, citing *Roe, supra*, the Court stated the issue before it as follows: "(W)hether the flat prohibition of saline amniocentesis is a restriction which 'reasonably relates to the preservation and protection of maternal health' ".<sup>116</sup>

The Court cited voluminous record evidence of the safety and effectiveness of saline amniocentesis, as compared with other available abortion procedures, and concluded that the state prohibition bore no reasonable relationship to the protection of maternal health. Significantly, in discussing the validity of the statutory prohibition of this particular medical procedure, the Court did not refer to any constitutional considerations of privacy. No such considerations were involved in the selection of that particular medical procedure by the patient and her physician. The procedure was evaluated by them and by the Court solely on the basis of the medical evidence of its safety and effectiveness.<sup>117</sup>

*Planned Parenthood* thus stands for the proposition that although a decision of whether to have an abortion is within the constitutional zone of privacy, deserving the protection provided by the "compelling interest" standard, the selection of a particular abortion procedure is a medical matter to which privacy status does not attach and which may be regulated by government, provided a rationale basis for such regulation exists.<sup>118</sup>

<sup>116</sup> *Id.* at 76.

<sup>117</sup> The voluminous record evidence discussed in Argument II, *supra*, on the safety and effectiveness of laetrile vis a vis the patient with life-threatening or terminal illness makes it clear that there is a reasonable relationship between the premarketing provisions of the Act and the public health and welfare.

<sup>118</sup> Similarly, in *Eisenstadt v. Baird*, 405 U.S. 438 (1972), where the Court held that unmarried individuals have a privacy right to purchase and to use contraceptives, the Court noted that the contraceptives themselves, if they are new drugs within the meaning of the Act would be subject to the premarket approval under Section 505, 21 U.S.C. § 355. *Id.* at 452. See also *Whalen v. Rose*, 429 U.S. 598 (1977).

In the instant case, the analogue of the right to decide whether to have an abortion is the right to decide whether to receive or forego cancer treatment. But although the decision whether to receive treatment may be constitutionally protected, the choice among treatment alternatives is not within the scope of the constitutional right to privacy. The issue is rather, whether "the regulation reasonably relates to the preservation and protection of maternal health."<sup>119</sup> Its analogue is whether the premarketing provisions of the Act reasonably relate to the preservation and protection of the health of the cancer patient.

#### E. The Governmental Interest In Protecting Individual Health And Public Health Provides Compelling Justification For The Application Of Pre-Marketing Requirements To Laetrile

Even where the Court has accorded "fundamental" constitutional protection to areas of private decision-making, it has recognized that those rights are not absolute; they may be limited by regulation serving compelling public purposes.<sup>120</sup>

##### 1. Protection Of Public Health

Protection of public health has always been accorded special recognition by the courts as providing compelling justification for state regulation. The Court itself has recognized that where public health and safety are at stake, even fundamental rights may be regulated and restricted under the states police power.<sup>121</sup>

While finding that the right of privacy is "broad enough to encompass a woman's decision whether or not to termi-

<sup>119</sup> *Roe v. Wade*, 410 U.S. at 163.

<sup>120</sup> See nn.94-97, *supra*.

<sup>121</sup> *Roe v. Wade*, 410 U.S. at 153-154, 162-163.



nate her pregnancy",<sup>122</sup> the Court in *Roe* maintained that at some point in the pregnancy the state's important interests in safeguarding health, in maintaining medical standards, and in protecting potential life become sufficiently compelling to sustain regulation of the factors that govern the abortion decision.<sup>123</sup> With respect to the health of the mother, the Court concluded that the "compelling" point is at approximately the end of the first trimester.<sup>124</sup> This conclusion was based on the medical fact that the risk of a woman's death in first trimester abortions appears to be at least as low as that in normal child birth,<sup>125</sup> while the increase in the hazards to abortion procedure in the second trimester justified imposition of state regulations. With respect to the state's interest in potential life, the compelling point was found to be at viability—which occurs approximately at the end of the second trimester. At this point the Court indicated that the state could even prohibit abortion except where necessary for the preservation of maternal life or health.<sup>126</sup>

These aspects of the holding in *Roe* are significant in light of the constitutional issue raised, for they reflect this Court's recognition of the government's compelling interest in protecting individual health, and in protecting the public health generally where individual conduct may adversely affect the well-being of others.<sup>127</sup> The authority

<sup>122</sup> *Id.* at 153.

<sup>123</sup> *Id.* at 154.

<sup>124</sup> *Id.* at 163.

<sup>125</sup> *Id.*

<sup>126</sup> *Id.* at 164-165.

<sup>127</sup> Even John Stuart Mill recognized that state regulation in the area of public health did not impermissibly infringe upon the choice of the individual. He contended that where, "there is a definite damage, or a definite risk of damage, either to an individual or to the public, the case is taken out of the province of liberty and placed in that of morality or law." J.S. Mill, *On Liberty* 100 (Liberty Arts Press 1956).

to protect individual health, and the public health generally, may be exercised to overrule the woman's personal decision to undergo a particular medical or surgical procedure during the second and third trimesters of pregnancy even when she is fully aware of the risks of the procedure, and is willing to take those risks.<sup>128</sup> An individual's decision to use Laetrile can stand on no higher constitutional level than the decision of a woman to have an abortion in the later stages of pregnancy.

The FDA seeks to prevent the use of Laetrile because its proponents have failed to meet the premarketing standards for drug approval which Congress established in Section 505 of the Act. The effectiveness standard, in particular, is designed to protect the public health by ferreting out "those drugs for which there is no affirmative, reliable evidence of effectiveness."<sup>129</sup> Laetrile falls within that class and its prohibition serves compelling public health purposes.

In the case of cancer, it has been established on the record that a significant number of patients can be cured or have their lives extended by the use of legitimate therapy, especially when treatment is begun as soon as possible after diagnosis. Ad. R. 173, 42 Fed. Reg. at 39798.<sup>130</sup> The availability of Laetrile serves to encourage delay among certain cancer patients in seeking effective therapy. 42 Fed. Reg. at 39799. Moreover, even among patients who begin treatment of their cancers with effective therapy, the readily acknowledged side effects of that therapy may cause them to cease to use such methods at a time when their application still may be successful, and turn instead to Laetrile—"the painless cure". 42 Fed. Reg. at 39799 and 39797. Because legitimate therapy

<sup>128</sup> 410 U.S. at 162-165.

<sup>129</sup> *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 616 (1973).

<sup>130</sup> See also statistics cited *supra* at notes 10, 30.

may be stopped, delayed or avoided, many cancer patients will die needlessly or prematurely; this fact alone provides compelling justification for prohibiting interstate transportation and sale of drugs such as Laetrile absent compliance with the premarketing standards.

**F. Consent To Treatment With An Unapproved Drug Does Not Override The Government's Interest In The Pre-Marketing Requirements Of The Act**

This Court has indicated that a patient's desire for and consent to a particular medical treatment would not be sufficient to override a statutory prohibition of the procedure where that prohibition reasonably relates to the preservation and protection of health.<sup>131</sup> Even where fundamental rights are at stake, this Court has held that compelling governmental interests will prevail over the interests of a consenting adult.<sup>132</sup> Together, the Court's rulings in *Planned Parenthood* and *Roe* indicate that the consent of a patient to treatment with Laetrile will not override the government's interest in the safety and efficacy provisions of the Act.

Further, measured against this record, the exercise of informed consent to take laetrile does not appear possible. Consent can only reach as far as the information it is based upon. For example, the federal regulations relating to informed consent<sup>133</sup> require that a patient be made aware of the benefits of a drug or its discomforts or risks. The district court's consent form does not provide for this information.<sup>134</sup> Further, this record, discussed *supra*, establishes not only that Laetrile is not generally recognized as safe or effective for any purpose, it also demonstrates that the lack of knowledge about

<sup>131</sup> See cases nn.97, 106, *supra*.

<sup>132</sup> *Id.*

<sup>133</sup> 45 Code of Federal Regulations 46.103.

<sup>134</sup> Ct.R. 409-414, 423-480, 1505 and attachments.

specific toxicity effects by oral and injection administration makes it impossible to put together a valid consent form for its administration.

**CONCLUSION**

Statutes should be given their fair meaning in accord with the evident intent of Congress. *See e.g., United States v. Sullivan*, 332 U.S. 698 (1948) and *United States v. Raynor*, 302 U.S. 540 (1938). The court of appeals by writing the terminally ill out of the statute and the district court by its clearly erroneous application of the grandfather exemption and its perversion of the concept of right to privacy protections have construed the federal drug laws and the Constitution in a way that conflicts with the plain meaning, statutory intent and Court interpretation. The course of action advocated by these courts erodes the protections provided by the federal drug laws and poses a significant threat, particularly to those whose illness is life-threatening instead of terminal. For these reasons, the Government's petition to this Court should be granted; the decisions below should be reversed; the decision of the Commissioner should be found to be supported and the courts below directed to adopt that decision as properly declaring the status of the drug Laetrile.

Respectfully submitted,

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March 8, 1979

# **Appendices**



## STATUTORY APPENDIX

*FOOD, DRUG AND COSMETIC ACT*

Section 201(p), 21 U.S.C. § 321(p), provides in part:

The term "new drug" means—(1) Any drug \* \* \* the composition of which is such that such drugs is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this chapter it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use.

\* \* \*

Section , 21 U.S.C. § 331(d) provides:

(d) the introduction or delivery for introduction into interstate commerce of any article in violation of section 344 or 355 of this title.

Section 505, 21 U.S.C. § 355, provides as follows:

(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug.

(b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which

have been made to show whether or not such drug is safe for use and whether such drug is effective in use \* \* \*

\* \* \*

(d) If the Secretary finds \* \* \*, that (1) the investigations, \* \* \* required to be submitted to the Secretary \* \* \*, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests \* \* \* do not show that such drug is safe for use under such conditions; \* \* \* (4) \* \* \* he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) \* \* \* there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) based upon a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application \* \* \*.

As used in this subsection and subsection (e), the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

\* \* \*

(i) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(1) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, or preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing.

Section 107(c) (4) of Public Law 87-781, 76 Stat. 798 ("1962 grandfather clause") provides:

In the case of any drug which, on the day immediately preceding the enactment date [October 10, 1962], (A) was commercially used or sold in the United States, (B) was not a new drug as defined by Section 201(p) of the basic Act as then in force [21 U.S.C. § 321(p)], and (C) was not covered by an effective [new drug] application under section 505 of that Act [21 U.S.C. § 355], the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

#### ADMINISTRATIVE PROCEDURE ACT

Section 10(e) of the Act, 5 U.S.C. § 706 provides as follows:

To the extent necessary to decision and when presented, the reviewing court shall decide all relevant

questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall—

(1) compel agency action unlawfully withheld or unreasonably delayed; and

(2) hold unlawful and set aside agency action, findings, and conclusions found to be—

(A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law;

(B) contrary to constitutional right, power, privilege, or immunity;

(C) in excess of statutory jurisdiction, authority, or limitations, or short of statutory right;

(D) without observance of procedure required by law;

(E) unsupported by substantial evidence in a case subject to sections 556 and 557 of this title or otherwise reviewed on the record of an agency hearing provided by statute; or

(F) unwarranted by the facts to the extent that the facts are subject to trial de novo by the reviewing court.

In making the foregoing determinations, the court shall review the whole record or those parts of it cited by a party, and due account shall be taken of the rule of prejudicial error.

## APPENDIX A

### IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF SOUTH CAROLINA SPARTANBURG DIVISION

Civil Action No. 76-1637

WILLIAM W. KING, JR.  
and BROADUS ALLISON,  
*Intervenors,*

IN RE:

JULIAN H. MORGAN, SR.  
and JULIAN H. MORGAN, JR.,  
*Plaintiffs,*

vs.

DAVID MATTHEWS, as Secretary of Department of Health, Education and Welfare; ALEXANDER M. SCHMIDT, Commissioner, Food and Drug Administration; and E. KENNETH AYCOCK, Commissioner, Department of Health and Environmental Control of State of South Carolina,

*Defendants.*

### ORDER

This is an action to restrain the defendants from interfering with plaintiffs'-intervenors'<sup>1</sup> (hereinafter referred to as plaintiffs) procurement of a substance known variously as Laetrile, Amygdalin, Prunasin or Vitamin B 17; to obtain civil, criminal and ethical immunity for physicians, nurses and technicians, who would handle and administer this substance; and for a Rule to Show Cause why plaintiffs should not be allowed to procure the sub-

<sup>1</sup> The intervenors were made parties to the action by this Court's Order of October 19, 1976.



stance and place it in the hands of a licensed physician. The remaining defendants<sup>2</sup> have moved for dismissal of the action and for summary judgment on the grounds that the Court lacks subject matter jurisdiction of the action, because plaintiffs have failed to exhaust their administrative remedies, and even if there is jurisdiction, the plaintiffs have not and cannot meet the burden required of them to justify the injunctive relief requested.

The matter was heard by the Court on October 19, 1976 subsequent to its issuance of a Rule to Show Cause why plaintiffs should not be granted the relief requested in their motion for an immediate hearing.<sup>3</sup>

Since this is essentially a proceeding for a preliminary injunction, the provisions of Rule 52(a) of the Federal Rules of Civil Procedure dictate that the Court make the following

#### FINDINGS OF FACT

1. Amygdalin is the chemical name for Laetrile, a substance which occurs naturally in the kernels of apricots, peaches, bitter almonds and in other plant materials. It is a member of a class of substances known as cyanogenic glycosides. Laetrile or amygdalin is also commonly referred to as "Vitamin B-17" although any nutritional value it might have as a vitamin has not been established.

2. There is not currently on file nor has there ever been on file with the Food and Drug Administration an

<sup>2</sup> The defendant Aycock, Commissioner of South Carolina Department of Health and Environmental Control was dismissed from the case with plaintiffs' agreement on his motion for judgment on the pleadings.

<sup>3</sup> Plaintiffs moved for an immediate hearing stating inter alia, as grounds the gravity of plaintiff, Julian H. Morgan, Sr.'s condition and asking for essentially the same relief prayed for in their complaint, in particular a preliminary injunction to prevent the ICC and the Customs Department from interfering with plaintiffs' transportation of a temporary supply of Laetrile.

approved new drug application (NDA) permitting the distribution in interstate commerce of amygdalin for administration into the human body.

3. There is not currently on file with the Food and Drug Administration a Notice of Claimed Investigational Exemption (IND) permitting the investigational use of amygdalin in humans. An IND application was last made in 1970 by McNaughton Foundations of California which application was found inadequate and terminated shortly after it was received.

4. The plaintiff, Julian H. Morgan, Sr., was suffering from the advanced stages of cancer of the prostate and had from time to time used the substance in question, Laetrile, in an attempt to treat this disease and to mitigate its effects. On October 26, 1976, he died of the disease. The intervenor, Broadus Allison, is afflicted with cancer and seeks to use Laetrile to mitigate its effects.

#### CONCLUSIONS OF LAW

Initially the defendants' challenge this court's subject matter jurisdiction on the basis that plaintiffs have failed to exhaust their administrative remedies in that the drug has never been submitted to the Food and Drug Administration (FDA) for its approval and thus it has not had the opportunity to rule on the merits of such an application. In light of the Court's ruling on the preliminary injunction, it is not necessary at this time to consider this issue.

In considering whether the Court should grant a preliminary injunction, the plaintiffs have the burden of showing: (1) the probability that the plaintiff will succeed on the merits; (2) the threat of irreparable injury to the plaintiff should preliminary injunctive relief be denied; (3) the lack of injury to other parties should the injunction issue; and (4) the public interest will not be harmed by the granting of the preliminary relief sought.

*Conservation Council of North Carolina v. Costanzo*, 595 F. 2d 498, 502 (4th Cir. 1974); *Long v. Robinson*, 432 F. 2d 977, 979 (4th Cir. 1970). The plaintiffs have not met their burden with regard to these factors.

First, and most significantly, they have failed to show a substantial likelihood of success on the merits; specifically, that Laetrile is not a "drug" within the meaning of 21 U.S.C. § 321(g)(1) which defines it to be an article "... intended for use in the diagnosis cure, mitigation, treatment or prevention of disease in man ...." It is the intended use of substance which determines whether or not it is a "drug". *Hanson v. United States*, 417 F. Supp. 30, 34 (D. Minn. 1976), aff'd *Hanson v. United States*, No. 76-1156 (8th Cir. August 26, 1976). The evidence presented here indicates that Laetrile was intended to be used to treat the plaintiffs for cancer and to mitigate its effects. Accordingly, there is little likelihood of success on this issue. Furthermore, plaintiffs have not shown a substantial likelihood of success with respect to whether Laetrile is a "new drug" within the meaning of 21 U.S.C. § 321(p)(1) which defines it as "any drug ... the composition of which is such that such drug is not generally recognized among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed ...." Plaintiffs have not shown a substantial likelihood of success in establishing that Laetrile is generally recognized as safe and effective by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs.

To the contrary, the defendants have presented substantial evidence, by affidavit and at the hearing, which shows that Laetrile is not generally regarded as safe and effective for use in the treatment of cancer.<sup>4</sup> Any

<sup>4</sup> Plaintiffs' own expert witness testified that it could not be said that Laetrile was generally recognized as safe and effective for

drug that is not generally recognized by qualified experts as safe and effective for its intended use is a new drug and cannot be shipped in interstate commerce until the information required by 21 U.S.C. § 355(b) is submitted for approval to the Secretary of Health, Education and Welfare in the form of a New Drug Application establishing that adequate and well controlled investigations have been performed to show that the drug is safe and effective, and the application is approved, 21 U.S.C. § 355. Here no NDA is or was in effect with respect to Laetrile.<sup>5</sup> See Finding of Fact 2, *supra*.

use in the treatment of cancer; rather, it was recognized by a few. The defendants' expert testified that Laetrile was not recognized by those qualified by training and experience to be safe and effective for use in the treatment of cancer. This is supported by the affidavits submitted by the defendants. See Affidavit of Robert C. Eyerly, M.D. at 3; Affidavit of Vincent T. DeVita, Jr., M.D. at 4; Affidavit of George J. Hill, II, M.D. at 4; Affidavit of Carl M. Leventhal, M.D. at 3.

<sup>5</sup> Plaintiffs apparently contend that the burden is on the FDA to approve or disapprove of a new drug in the first instance, since they complain that the FDA "has failed, without adequate explanation, to approve Laetrile for distribution and use in the United States. ..." The language and the history of the Act demonstrate that it is not the responsibility of the FDA to initiate applications on its own in the absence of an application that conforms with the statutory requirements of § 505(a) and (b). No such application has been filed here. See Finding of Fact 2, *supra*.

The FDA has been given the responsibility of "approving applications". Therefore, it is apparent that they must be submitted for approval. This conclusion conforms with the Act's legislative history.

The House Committee Report in discussion § 505 during its initial drafting in 1938 stated that

This provision will not put the Federal Government into the business of developing new drugs, nor will it require the Government to duplicate laboratory and clinical tests made by responsible manufacturers. The provision merely sets up a method for the authoritative review of the manufacturer's tests and will not unreasonably delay the introduction of new drugs in the market.

H.R. Rep. No. 2139, 75th Cong., 3rd Sess. (April 14, 1938), p. 9. Further discussion was had as to this section in the House Report

The facts indicate that the administrative process has not been followed and since this would likely preclude an award of relief at the end of the litigation, the plaintiffs have not made a sufficient showing of the probability of ultimate success on the merits to obtain a preliminary injunction. *Wallace v. Lynn*, 507 F.2d 1186, 1189 (D.C. Cir. 1974).

It has not been shown that the plaintiffs will suffer irreparable harm if the injunction is not forthcoming. The only evidence presented to this Court of any benefit Laetrile might provide in the treatment of cancer is that in some instances individuals taking it "seem to experience diminishing pain and an increase in appetite, weight gain, and psychological improvement." Affidavit of Raymond Hilliard, M.D.<sup>6</sup> This is consistent with the effect a placebo would produce. The record is devoid of any evidence that Laetrile cures or halts the progress of cancer. Thus it does not follow that the enforcement of a law which denies Laetrile to a victim of cancer will cause him to suffer irreparable harm.

Finally, it has not been shown that the granting of injunctive relief in this case would not injure other parties or the public. To the contrary, to permit the distribution of Laetrile in this case would be to circumvent the laws enacted to assure that drugs distributed in interstate commerce be both safe and effective for their recommended use, and would undermine the ability of those charged

of the 1962, amended version, which indicates that application was to be made by the manufacturer:

Section 505 of the Food, Drug and Cosmetic Act prohibits interstate shipment of a "new drug" . . . unless it is first cleared for safety through the filing of a new drug application by the manufacturer.

H.R. Rep. No. 2464, 87th Con., 2d Sess. (Sept. 22, 1962), p. 3.

<sup>6</sup> Testimony to this effect was also given at the hearing by Dr. Hilliard and by the plaintiff Julian H. Morgan, Jr.

with upholding these laws to do so most effectively in the future. Such a holding would also provide any future proponent of unproven remedies a basis for arguing to another court that it should allow the distribution of substances in a manner contrary to the law.

This Court is not unmindful of the gravity of the situation facing those who are afflicted with cancer and of their desire to choose their own remedies in view of the absence of any known cure for this disease. However, granting the relief requested in this case could not only harm the public by weakening laws calculated to prevent the victimization of those afflicted with cancer and other conditions by playing on their desperation in the marketing of unproven and, possibly worthless remedies, but it could also further the growing tendency of those afflicted with this disease to engage in self treatment resulting in a delay in seeking early diagnosis and prompt treatment with forms of therapy that have established value. The result of this type of delay could be disastrous, since early diagnosis and treatment is of the utmost importance in the management of cancer.<sup>7</sup>

<sup>7</sup> This is support by most of the affidavits before the Court. See Affidavit of Robert C. Eyerly, M.D. at 3-4; Affidavit of Carl M. Leventhal, M.D. at 4.

[P]roponents of Laetrile have advanced the argument that patients should be able to exercise free choice and select the drug if they wish to try it, despite a lack of scientific evidence of effectiveness. The idea that patients are able to make effective choices concerning cancer management without regard to existing evidence is dangerously misleading. Cancer management is a complex and demanding medical problem that depends upon availability of skilled trained physicians, surgeons, and other health professionals, and upon availability and use of drugs and other forms of therapy with defined and documented value. Availability and use of drugs which have not been found to have objective value makes no contribution to cancer management. It can, in fact, interfere with the very measures that are known to save lives by delaying diagnosis and effective treatment. The consequences of such delay may be needless and untimely death.

Affidavit of George J. Hill, II, M.D. at 3.



12a

Accordingly, plaintiffs' prayer for preliminary injunctive relief is denied.

AND IT SO ORDERED.

ROBERT F. CHAPMAN  
United States District Judge

November 30, 1976

Greenville, S.C.

13a

APPENDIX B

VERDICT OF CORONER

(WITHOUT INQUEST)

IN THE MATTER OF THE DEATH OF

JO ANNE ETTA PYE Deceased.

I, C.R. Simmons, Coroner of Alameda County, do certify:

That on the 1st day of February 19 79, I investigated the circumstances surrounding the death of the above mentioned person, caused an examination and identification to be made of the body and find that deceased was named

JO ANNE ETTA PYE

a white female, single, married, widowed, divorced, aged about 42 years; that she came to her death on the 3rd day of December 19 78 at Vesper Memorial Hospital, Emer. Room, San Leandro, Alameda County, California;

and that death was caused by cyanide intoxication suffered at undetermined hours on December 3, 1978, at 14425 Birch Street, San Leandro, California.

Jo Anne Etta Pye, a carcinoma patient, ingested an amount of laetrile, causing cyanide intoxication.

Ethyl alcohol - - - 0% (blood).  
Barbiturates - - - 0 MG% (blood).  
Cyanide - - - - 3.8 mcg/ml (blood) ; 0.8 mcg/ml (vitreous)  
175 mcg (total gastric).  
Diazepam - - - - 0.3 mcg/ml (blood)  
Desmethyldiazepam - 0 (blood).  
Caffeine - - - - 6.4 mcg/ml (blood).  
All other toxicological tests were negative.

I find death ACCIDENTAL.

CODE: N.A.

Identified by Robert Pye, ex-husband.

Investigation by J.L. Shaw, Deputy Coroner.

Autopsy Inspection by P.W. Hermann, M.D.

cc: San Leandro P.D., Att: Homicide  
Inst. Forensic Sciences

IN WITNESS WHEREOF, I have hereunto set  
my hand this 1st day of February 19 79.

*C.R. Simmons*  
C.R. Simmons

**CERTIFICATE OF DEATH**  
**STATE OF CALIFORNIA**

78-2563

[illegible]

## AMENDMENT OF MEDICAL AND HEALTH SECTION DATA-DEATH

[illegible]

16a

PYE		Joann		Natural		78-2563	
AKA		PYE		Joann		78-2563	
DATE OF BIRTH		11 Feb 1936		DATE REPORTED		12-3-78	
TIME REPORTED		1740		REPORTED TO		AT	
SEX		F		RACE		Cau	
AGE		42		WEIGHT		116	
HEIGHT		52		EYES		Brn	
HAIR		Brn		SOCIAL STATE		Divorced	
OCCUPATION		At Home		REMOVED BY		JLS/gj	
ON DUTY DEATH		NO		RELATIONSHIP		Wife	
DATE DEATH		12-3-78		TIME DEATH		1730	
DATE FOUND				TIME FOUND			
EST. DATE DEATH				FOUND BY			
PLACE OF DEATH		Vesper Memorial Hospital ER		CITY		S/Leandro	
ADDRESS OF DECEASED		14425 Birch Street 352-6851		STATE		Calif.	
FURNAL DIRECTOR		Guerrero Mortuary		BODY TEMP		Warm	
POLICE SCENE		NO		DEPARTMENT		S/L PD	
RELATIONSHIP		NAME		ADDRESS		CITY OR TELEPHONE	
EX-HUSB		PYE, Robert R.		582-8439		20111 Westridge Ct. #30 C/Valley	
DOCTOR		BRIDE, Francis (pronounced)				Vesper Mem Hospital	
NURSE		SHARP, Robin RN		(I)		Vesper Mem Hospital	
MEDICAL SUMMARY		Private physician _____ M.D. (will) (will not) sign death certificate.					
TREATMENTS - MEDICATIONS		CANCER OF THE BREAST					
INJURIES - DIAGNOSIS		Dec last seen by a Dr HESS in Chula Vista (714 421-0584) 10 weeks ago. She was also treated at the Richardson Clinic in Albany, in Mexico and the Philippines. Dec went into convulsions at home just prior to admit to ER. On special diet of natural foods and juices.					

PARTICULARS SURROUNDING DEATH (details, equipment in use, circumstances at, and leading to death.)

FAMILY of deceased notified on 12-3-78 at \_\_\_\_\_ TIME \_\_\_\_\_ via \_\_\_\_\_ Hospital

The Dec was brought to the ER at 1707 hours via police ambulance: she was pronounced at 1730 hours by Dr. Bride - the ER chart had a notation of 'essentially DCA'. Just prior to the calling of the ambulance, the Dec had gone into a state of convulsions. She had a history of cancer of the breast - diagnosed in various places - refused to have any type of operation.

The ex-husband reports that the Dec was probably last seen about ten weeks ago by her doctor in Chula Vista; she had no PMD in the local area. The Dec had been treated in Mexico and in the Philippines and had consulted various spiritual and faith healers. She was also treated in Albany at the Richardson Clinic. The Dec was being taken care of by a Gail WALZ who reports that the Dec was on a diet of natural foods and juices. She was taking various other medications prescribed by Dr. HESS including the medication made from apricot pits.

## INVESTIGATOR'S REPORT

Alameda County Coroner's Department  
Alameda County, California

Investigator: J.L. Shaw 132

INVESTIGATION	1800	TO	1845	TOTAL	.45
REPORTS	2015	TO	2030	TOTAL	.15

17a

PYE		Joann		Natural		78-2563	
INFORMANT NAME		Richardson Center-514 Kains Ave.		ADDRESS		Albany, Ca.	
KEMTER, Joanna		Richardson Center-514 Kains Ave.		CITY OR TELEPHONE		527 3020	
ERODIE, W. D.							
ILARS		12-05-78		1230 hrs.			
<p>as above (I) gave the following information: Dec'd initially seen in their clinic in March of '78. Meds include "amracycline, tamoxifen (discontinued), parocarb, dilauid, and laetrile. Dec'd had been seen by Dr. A.B. CAMERON (dept. of surgery) in March of '78 at Kaiser Hosp. in Hayward. A biopsy performed at Eden Hosp. "infiltrating adenocarcinoma of left breast".</p> <p>Lepraning of laetrile: In the beginning dec'd was given 9 Grams (30cc) every day for 20 days started 3-21-78; then 3 Grams (10cc) given 3 times a week for a month, then 2 times a week for a month, then 1 time a week (each dosage was 3 Grams or 10cc) for at least 16 months (dec'd never completed last stage). Last injection dec'd received was on Sept. 2th of '78. If the dec'd is unable to receive her weekly injection she takes a tablet of laetrile (1000 mgm). R/P does not know how many tablets the dec'd may have had on her person. When the dec'd returned home from the PI she was very depressed over prices and cost of food; loss of sleep associated with severe pain. Dec'd last seen at the clinic on the 28th of Aug., 1978. Laetrile tablets ordered through Mexico with affidavit.</p>							
SUPPLEMENTAL				Investigator: HLA #136			
INVESTIGATOR'S REPORT				Alameda County Coroner's Department			
Alameda County, California				INVESTIGATION			
				TIME FROM: TO TOTAL			
				REPORTS			
				TIME FROM: TO TOTAL			





# COUNTY OF ALAMEDA

OFFICE OF  
CHARLES R. SIMMONS  
CORONER-PUBLIC ADMINISTRATOR-PUBLIC GUARDIAN  
CONSERVATOR  
480 - 4TH STREET  
OAKLAND, CALIFORNIA 94607

PUBLIC ADMINISTRATOR  
PHONE: 874-8741

PUBLIC GUARDIAN-CONSERVATOR  
PHONE: 874-8741

CORONER'S DIVISION  
PHONE: 874-5551

cc: Vesper Memorial Hospital ER

Coroner  
Alameda County

Body of JO ANNE ETNA PYE

Autopsy performed upon the body of JoAnne Etta Pye at the Coroner's Office,  
480 - 4th Street, Oakland, California, on December 4, 1978, at 10:00 a.m., by  
Paul W. Herrmann, M.D.

## ANATOMICAL DIAGNOSES

- 1) CARCINOMA OF THE LEFT BREAST.
- 2) METASTASES TO THE LEFT AXILLARY LYMPH NODES,  
INTERNAL MAMMARY LYMPH NODES, AND INVASION OF  
THE CHEST WALL.
- 3) CARCINOMA OF THE RIGHT BREAST, PROBABLY METASTATIC.
- 4) CARCINOMA INVOLVING THE SOFT TISSUE OF THE RIGHT  
AXILLA.
- 5) ACUTE CONGESTION AND EDEMA OF THE LUNGS.
- 6) ACUTE CONGESTION OF THE LIVER AND KIDNEYS.
- 7) CYANIDE ODOR TO THE BODY CAVITY.
- 8) FATTY CHANGE OF THE LIVER.

CAUSE OF DEATH: CYANIDE INTOXICATION.

78-2563

## APPENDIX C

### COMMONWEALTH OF MASSACHUSETTS

### SUPERIOR COURT

Civil Action No. 78-6816

PLYMOUTH, SS.

CUSTODY OF A MINOR

### ORDER

The attorney for the child and the Attorney General have petitioned this Court to hold the parents in civil contempt as a result of the actions of the parents in removing the child from the Commonwealth of Massachusetts. Based on the stipulated evidence that the parents have in fact removed the child from the Commonwealth, and based on the fact that the parents are represented at this hearing by counsel, I find the parents to be in civil contempt of court for their violation of the Order that was entered on April 18, 1978 and that was incorporated into the Order entered on January 22, 1979, which directed that the child be treated by any board certified pediatric hematologist within the Commonwealth of Massachusetts. I continue the hearing to Wednesday, February 7, 1979, to permit the parents to cure the contempt.

The Court wishes to emphasize the ability of the parents to purge themselves of this contempt and thereby to avoid being subject to any penalty by returning the child to the Commonwealth of Massachusetts and complying fully thereafter with the Court's orders.

The Court has accepted into evidence today a new laboratory test which indicates a level of free cyanide in the child's blood at twice the normal level. In light of this

new evidence of chronic cyanide toxicity, and in light of the Court's belief that the parents share the Court's deep concern for the safety and well-being of the child, I would hope and expect that the parents will appreciate the medical and legal advisability of returning the child to the skilled supervision of a Massachusetts medical center—both to avoid being penalized for their contempt and to maximize the child's chances of being cured.

/s/ Guy Volterra  
GUY VOLTERRA, DCJ  
(Sitting by Statutory  
Designation)

Dated: January 31, 1979

COMMONWEALTH OF MASSACHUSETTS

SUPERIOR COURT

Civil Action No. 78-6816

PLYMOUTH, SS.

CUSTODY OF A MINOR

INTERLOCUTORY ORDER

As the Court finds, after extensive hearing, that the parents have been administering to the minor child an unapproved drug, Amygdalin (Laetrile), which is dangerous to health, and that the parents have also been giving the minor child without medical supervision and prescription megadoseages of Vitamins A and C, mineral supplements, enzymes, folic acid, and calcium lactate, and as the Court further finds that the administering of these substances and drugs has been against the specific advice of the treating physician; the Court finds that the conduct of the parents in administering these substances to the minor child is harmful to the health of the child and may be counter-productive to the medical treatment the child is currently receiving for acute lymphocytic leukemic. The Court, until entry of a Final Order, issues the following Interlocutory Order:

1. The Order of this Court for Care and Protection dated April 18, 1978 is hereby continued in force; and
2. The parents are hereby ordered to cease administering to the minor Amygdalin (also known as Laetrile, Vitamin B-17, Kemdalin, and other trade names) by tablet or injection to the minor; and
3. The parents are hereby ordered to cease administering to the minor Vitamin A and Vitamin C in any form and in any amounts except that which the minor

child may ingest from the diet recommended by the treating physicians; and

4. The parents are hereby ordered to cease administering to the minor enzyme enemas; and

5. The parents are hereby ordered to cease administering to the minor any mineral supplements, enzymes, folic acid, or calcium lactate unless the administration of such substances is first approved by the treating physician; and

6. The parents are ordered to submit the minor to such urine thiocyanate and serum thiocyanate tests as are ordered by the treating physician. The treating physician shall report to the Court any test results which indicate to him that the child remains at risk of chronic cyanide poisoning; and

7. The parents are ordered to submit the minor to such Vitamin A and liver function tests including SGOT, as are ordered by the treating physician to test for hypervitaminosis A and liver functions. The treating physician shall report to the Court any test results which indicate to him that the child remains at risk of hypervitaminosis A and impaired liver function.

8. The parents are to obtain from the treating physician a recommended diet prepared by a dietician which is nutritionally sound and which is to reflect the parents stated preference for natural foods which are free from additives and preservatives.

By the Court,

/s/ Guy Volterra  
GUY VOLTERRA, D. C. J.  
Sitting by Statutory  
Designation

Dated: January 22, 1979

# APPENDIX D

## IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF MARYLAND

No. K 77-1283

UNITED STATES OF AMERICA,  
*Plaintiff,*

v.

Articles of drug consisting of the following:

45 bottles (vials), more or less, and 47 bottles (vials)  
more or less, labeled in part:

(bottle (vial))

"Amigdalina Cyto Pharma \* \* \* 250 Comprimidos \* \* \*  
500 mg. \* \* \* Mexico"

(tablet)

Embossed on one side with "500" and other side is with  
a score mark and a pine tree logo.

23 boxes, more or less, and 25 boxes, more or less, each  
containing 100 ampuls, more or less, labeled in part:

(ampul)

"Amigdalina Cyto Pharma 10 ml. \* \* \* Cyto Pharma De  
Mexico S.A."

*Defendant.*

## COMPLAINT FOR FORFEITURE

To The Honorable Judge of the United States District  
Court For The District of Maryland.

Now comes the United States of America by Jervis S.  
Finney, United States Attorney for the District of Mary-  
land, and shows to the Court:



1. That this complaint is filed by the United States of America, and prays seizure and condemnation of certain articles of drug, as hereinafter set forth, in accordance with the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).

2. That this Court has jurisdiction under 28 U.S.C. 1345 and 21 U.S.C. 334.

3. That there are at Baltimore, Maryland, in the possession of Henderson's Pharmacy, 7401 Harford Road, and Robert W. Henderson, 5 Weyburn Court, Baltimore, Maryland, or elsewhere within the jurisdiction of this Court, the articles of drug hereinabove described in the caption of this matter, which articles were shipped in interstate commerce on or about July 12, 1977 (47 bottle (vial) and 23 box lots) and on or about July 21, 1977 (45 bottle (vial) and 25 box lots), by Cyto Pharma, from Tijuana, Mexico into California via known carriers; and subsequently delivered to Robert W. Henderson in Baltimore, Maryland.

4. That the aforesaid articles are new drugs within the meaning of 21 U.S.C. 321(p)(1), which may not be introduced or delivered for introduction into interstate commerce pursuant to 21 U.S.C. 355(a), since no approval of an application filed pursuant to 21 U.S.C. 355(b) is effective with respect to such drugs; no notice of claimed investigational exemption pursuant to 21 U.S.C. 355(i) and regulation 21 CFR 312.1 is on file for such drugs; and the drugs are not exempt from the requirements of the new drug provisions of said act, 21 U.S.C. 355, pursuant to the order of the Court in *Rutherford v. United States*, 429 F. Supp. 506 (W.D. Okla., 1977), since the articles were offered for importation into the United States solely for the personal use and benefit of persons who executed affidavits required by the Court in *Rutherford* and are intended for distribution to per-

sons other than those for whose benefit the articles were imported.

5. That the aforesaid articles were adulterated when introduced into and while in interstate commerce, within the meaning of said Act, 21 U.S.C. 351(a)(2)(B) in that they are drugs and the methods used in, and the facilities and controls used for, their manufacture, processing, packing, and holding did not conform to and were not operated and administered in conformity with current good manufacturing practice, as set forth in regulations 21 CFR 211, to assure that such drugs meet the requirements of said Act as to safety and have the strength and meet the quality and purity characteristics which they purport and are represented to possess.

6. That the aforesaid article (47 bottle (vial) lot) was adulterated when introduced into, while in, and while held for sale after shipment in interstate commerce, within the meaning of said Act, 21 U.S.C. 351(c), in that it is a drug not subject to the provisions of 21 U.S.C. 351(b) and its strength differs from that which it purports and is represented to possess, because it contains less than 500 milligrams of amygdalin.

7. That the aforesaid articles were misbranded, when introduced into, while in, and while held for sale after shipment in interstate commerce, within the meaning of said Act, 21 U.S.C. 352(j), in that Amigdalina (amygdalin) tablets are dangerous to health when used in the manner, and with the frequency and duration prescribed, recommended and suggested in the labeling thereof, that is, when used orally and with the frequency and duration prescribed in affidavits which are accompanying labeling for the tablets.

8. That by reason of the foregoing, the aforesaid articles are held illegally within the jurisdiction of this Court, and are liable to seizure and condemnation.

WHEREFORE, plaintiff prays that process in due form of law according to the course of this Court in cases of actions in rem issue against the aforesaid articles; that all persons having any interest therein be cited to appear herein and answer the aforesaid premises; that this Court decree the condemnation of the aforesaid articles and grant plaintiff the costs of this proceeding against the claimant of the aforesaid articles; that the aforesaid articles be disposed of as this Court may direct pursuant to the provisions of said Act; and that plaintiff have such other and further relief as the case may require.

UNITED STATES OF AMERICA

By: /s/ Jervis V. Finney  
United States Attorney

/s/ Gerard P. Martin  
GERARD P. MARTIN  
Assistant United States Attorney

8/4/77

I certify under penalties of perjury that the facts contained in the aforesaid complaint are accurate and true to the best of my knowledge and belief.

/s/ Gerard P. Martin  
GERALD P. MARTIN  
Assistant United States Attorney

IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF MARYLAND

No. K-77-1283

UNITED STATES OF AMERICA,  
*Plaintiff,*

v.

Articles of drug consisting of the following:

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500 mg. \* \* \* Mexico"

(tablet)

Embossed on one side with "500" and other side is with  
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23 boxes, more or less, and 25 boxes, more or less, each  
containing 100 ampuls, more or less, labeled in part:

(ampul)

"Amigdalina Cyto Pharma 10 ml. \* \* \* Cyto Pharma De  
Mexico S.A."

*Defendant.*

MOTION FOR PARTIAL RELEASE OF  
SEIZED GOODS AND SUPERVISED  
DELIVERY TO CERTAIN PATIENTS

Now comes the United States of America, plaintiff herein, and moves this Honorable Court for release of certain ampoules and tablets of the drug Laetrile, as hereinafter specified, which were seized by the United States Marshal on August 5, 1977 pursuant to motion of

the Court. The order prayed for seeks release from the United States Marshal of limited amounts of the drug for redelivery to Robert Henderson, R.Ph., 7401 Harford Road, Baltimore, Maryland, in order that Mr. Henderson, under supervision of authorized agents of the United States Food and Drug Administration, cause to be delivered to patients entitled to receive Laetrile the amount of said drug they ordered. As grounds for this motion plaintiff states that:

1. Pursuant to procedures authorized by the Court in *Rutherford v. United States*, 429 F. Supp. 506 (W.D. Okla., 1977), persons diagnosed as suffering from terminal cancer may import for their personal use only a limited amount of Laetrile not to exceed 750 tablets and 150 10cc ampoules. As a condition precedent to importation the patient or his duly authorized agent must present to the United States Customs Service an affidavit of a physician certifying the patient's condition and specifying the amount of Laetrile ordered.

2. On July 12, 1977 affidavits for 16 patients were presented to customs officials to justify importation of 2,380 ampoules and 11,950 tablets of Laetrile. These articles were thereafter shipped to Robert Henderson.

3. On July 21, 1977 affidavits for 17 patients were presented to customs officials to justify importation of 2,450 ampoules and 11,150 tablets of Laetrile. These articles were thereafter shipped to Robert Henderson.

4. As agent for the persons named in the affidavits, Mr. Henderson was authorized to deliver to these persons the amounts of Laetrile imported on their behalf and for their personal use.

5. Investigations by United States Food and Drug Administration investigators have revealed that the affidavits are fraudulent in that patients on whose behalf affidavits were presented to customs officials either or-

dered significantly less than the amount of Laetrile declared on the affidavits or did not order any Laetrile whatsoever and are unaware of any affidavit being executed on their behalf.

6. Food and Drug Administration investigations further reveal that Mr. Henderson has solicited abandonment of Laetrile from patients who ordered Laetrile and on whose behalf affidavits were presented to customs officials and that either as a result of such solicitations or for other reasons, some patients have cancelled or reduced their orders for Laetrile.

7. Food and Drug Administration investigations further reveal that affidavits presented to customs officials contain false information in that the amounts of Laetrile represented to have been ordered by the patients exceeds the amounts actually ordered and that Mr. Henderson uses these amounts of Laetrile not ordered by patients to create a stockpile from which he then sells to other persons who have not executed affidavits presented to Customs for purposes of facilitating importation of the drug for their use.

8. Patients on whose behalf Laetrile was lawfully imported into the United States pursuant to procedures prescribed in *Rutherford v. United States*, *supra*, have supplied FDA investigators with information concerning the amounts of Laetrile they ordered and still desire to be delivered to them. In the aggregate the total amount of Laetrile they ordered and desire to receive is 77 ampoules and 280 tablets.

The Food and Drug Administration is in the process of contacting other patients to determine the amounts of Laetrile they ordered and still desire to obtain and will report promptly its finding to this Court.



30a

Wherefore, the United States prays that the Court enter the attached proposed Order for Partial Release of Seized Goods and Supervised Delivery to Certain Parties.

Respectfully submitted,

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No. 78-605

Supreme Court, U. S.  
FILED

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MICHAEL RODAK, JR., CLERK

**In the  
Supreme Court of the United States**

OCTOBER TERM, 1978

UNITED STATES OF AMERICA, et al.,

*Petitioners,*

VS.

GLEN L. RUTHERFORD, et al.,

*Respondents.*

On Writ Of Certiorari To The United States Court  
Of Appeals For The Tenth Circuit

**BRIEF OF THE NATIONAL HEALTH FEDERATION,  
AMICUS CURIAE, IN SUPPORT OF RESPONDENTS**

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**BRIEF OF THE NATIONAL HEALTH FEDERATION,  
AMICUS CURIAE, IN SUPPORT OF RESPONDENTS**

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**The National Health Federation  
and Laetrile Availability**

The National Health Federation is a California not-for-profit corporation, and is America's largest, non-commercial health consumer group. It was founded in 1955, and its membership is comprised of men and women in all walks of life, belonging to a variety of religious faiths and

political persuasions, and engaged in nearly every profession and trade. Its members believe that health freedoms are inherently guaranteed to us as human beings, and our right to them as Americans is implied in the words, "life, liberty and the pursuit of happiness". The National Health Federation and the 80,000 or more persons it represents oppose monopoly and compulsion in matters related to health and nutrition. In particular, the Federation and its membership believe in the "freedom of choice" now, and always, exercised by American citizens as to their health, and oppose "medical dictation" of any type whatsoever from Washington, D.C., or elsewhere.

"Freedom of choice", when applied to the instant cause, encompasses the freedom of the terminally ill, members of the respondent class, and, in fact, everyone, to choose between existing therapies for the treatment of cancer.

The Federation also believes that such choice between the highly toxic and largely ineffective orthodox cancer therapies, and the non-toxic therapy of treatment with Laetrile, as included in an overall "metabolic therapy" program, lies within the Constitutionally protected right of privacy, allowing members of the Respondent class, and others, to make said choice free from government intervention, and bureaucratic dictation.

Accordingly, The National Health Federation, in light of its long-standing involvement with the issues encompassed herein as to freedom of choice, the primary principle upon which said organization was founded, presents its brief *amicus curiae*.

## **SUMMARY OF THE ARGUMENT**

### **Lower Court Decisions**

The lower Court decisions herein quite properly protect the respondent class of terminal cancer patients from FDA interference with their use of Laetrile.

### **Cancer — The Underlying Problem**

The federal government's own statements and statistics demonstrate that we are not winning the battle against cancer, but losing it very rapidly, the conventional therapies being totally inadequate to handle the problem.

### **Petitioner Discriminates with a "Double Standard" of Safety**

Whether or not due to its implacable opposition to Laetrile over the years, FDA has not even-handedly and non-discriminatorily applied to Laetrile the same standards by which it has measured other anti-cancer drugs for "safety" and "efficacy", thereby approving many very toxic, grossly dangerous, even lethal and fatal drugs in the name of "safety".

### **"Consensus of Ignorance" No Substitute for Scientific Expertise**

No provision of the Federal Food, Drug, and Cosmetic Act provides that merely because "experts" know nothing of a substance, that this obviates "general recognition" by those who are actually qualified to express an opinion.

### **Laetrile — No Issue as to Its Chemical Identity**

The Commissioner himself, in his decision on the status of Laetrile, recognized that the term Laetrile is used interchangeably with amygdalin, nitriloside, and Vitamin B-17.



### **No "Efficacy" Requirement — 1962 Grandfather Clause**

FDA's attempt to read efficacy into the requirements of the 1962 grandfather clause would lead to the anomalous result that an individual suffering from a life-threatening disease for which there exists no known "effective" treatment, would not be lawfully entitled to any treatment at all since no drug could qualify under FDA's interpretation of the Act.

### **FDA Ignores Value of Laetrile**

FDA ignores recognized clinical investigations denoting the value of Laetrile.

### **FDA Attempts to Destroy State Laws by Bureaucratic Fiat**

FDA ignores, and by silence implies the nonexistence of a very important circumstance, namely the passage by nineteen States thus far of laws specifically permitting and approving the use of Laetrile.

### **Laetrile Denied to the States**

The state Laetrile laws thus far enacted will have little actual value due to the breadth and scope of the commerce clause.

### **FDA Opposition to Laetrile Not Based Upon Science**

FDA opposition to Laetrile has precluded a scientifically based review by the Agency.

### **Respondent Rutherford, et al. — No Means or Resources To Follow "New Drug" Procedures**

Lack of resources and time, due to the terminal nature of his disease, preclude the terminally ill cancer patient

from pursuing FDA's "New Drug Application" procedures.

### **Important Constitutional Rights Involved**

The FDA has failed to exhibit a "compelling state interest", in order to justify the interference with respondents' Constitutionally protected rights of privacy.

### **Individual Rights Recognized by Court Below**

The U. S. District Court properly recognized and applied guaranteed Constitutional rights of privacy to the case at bar.

### **FDA Reaches Back to the Middle Ages to Ban Laetrile**

FDA's review of Drug Regulation in its "Appendix A" is inapropos and ignores the numerous instances wherein bureaucracy has deprived mankind of progress in the drug field.

## ARGUMENT

### Lower Court Decisions

Elsewhere herein the Court has been duly advised of the decisions of the U. S. District Court for the District of Oklahoma and the U. S. Court of Appeals for the Tenth Circuit, respectively, whereby such decisions protect the respondent class of terminal cancer patients from interference by FDA as to the Laetrile which they value very highly. Indeed, certain persons in such class, such as respondent Glen Rutherford, depend upon the same for their very lives.

Heretofore the U. S. District Court for the District of Oklahoma, Honorable Luther Bohanon presiding, has ruled extensively concerning the legal status of Laetrile, these rulings having followed a so-called "rule-making" proceeding of FDA, previously ordered by the U. S. Court of Appeals for the Tenth Circuit and the U. S. District Court in prior rulings, and reluctantly acceded thereto by FDA.

The December, 1977 opinion of the District Court (Pet. App. 11-44A) is reported at 438 F. Supp. 1287, and was, in summary:

1. That Laetrile, on October 9, 1962 (and, therefore, thereafter) was "generally recognized as safe" and met the other criteria of the 1962 "Grandfather Clause" to the Federal Food, Drug, and Cosmetic Act, and therefore is a drug proper and legal for distribution in interstate commerce.

2. That there is a Constitutional "right of privacy" which attaches to Respondent Glen Rutherford, and the others of the class action group of plaintiffs who have

brought the within action, as well as to those not specifically members of that class, which bars FDA from interfering with their use of Laetrile.

The Federation considers the U. S. District Court opinion and ruling in question to be well-reasoned, exhaustive and definitive in all respects, and adopts the ruling of said lower Court in all respects as though set forth herein in full in this amicus curiae brief.

The Federation further notes to the Court that FDA herein does not seek to limit availability of Laetrile to terminal cancer patients, or even any other designated class of persons, but by the ruling it seeks from this Court would bar Laetrile to everyone, no matter what their position or condition.

If the petitioner agency is successful herein in its plea to the Court, namely that no one, not even a terminal cancer patient, may receive Laetrile in any form, thousands of patients now dependent upon Laetrile, and presently protected by the decrees of the District Court below and the 10th Circuit U. S. Court of Appeals, will be effectively left to die without the treatment they now value for their very lives.

### Cancer — The Underlying Problem

Basic to the arguments being presented to the Court by petitioner herein is the "rosy", but totally unjustified "imputation" that with orthodox, or conventional, cancer therapies we are rapidly winning the battle against cancer, and that, therefore, we need look no further to such therapies as those afforded by Laetrile, and its accompanying metabolic therapies as employed by physicians throughout the United States, and over the World. However, the government's own statements and statistics demonstrate that

we are not winning the battle against cancer, but losing it very rapidly, the conventional therapies being totally inadequate to handle the problem.

In 1977, 400,000 Americans died of cancer, a figure which is seven times the total fatalities in the Vietnam and Korean wars. According to Dr. Marvin Schneiderman, Associate Director of the National Cancer Institute, a government agency which receives approximately \$800,000,000.00 per year in taxpayers' funds, the death rate from all types of cancer is continuing to increase. Dr. Schneiderman also states that cancer mortality, overall, is increasing, so that it is the only major cause of death which has continued to rise from 1900 through 1976. Putting it another way, more people are dying today from cancer in every age group than have died from cancer in such age groups at any other time in American history. According to present projections 1 in 4 Americans is doomed to die of cancer. Pursuant to the best available government statistics, the cancer death rate in 1900 was 64 per 100,000 of the population, a figure which has now increased to 162.8 per 100,000, or almost a three-fold increase. As recently as 1965, the cancer death rate per 100,000 persons was only 127.9. Within the overall statistics, there are equally unfavorable figures as to specific types of cancer. For example, between 1973 and 1975, the number of lung cancer cases increased in the United States 13%, breast cancer, 17%, stomach cancer, 28%, and prostate cancer, 32%, for the same period. Nor is median survival time particularly encouraging for the cancer sufferer. According to the U. S. Department of Health, Education, and Welfare, the observed median survival time in approximately 219,500 cases of cancer (all sites) was 1.7 years. This median survival time includes those cases wherein a cancer is localized, or limited to the site of origin.

Of great interest to the matter at bar, however, are the statistics concerning distant (disseminated or "metastasisized") cancer, wherein the U. S. Government has stated that the five-year relative survival rate ranges from a maximum of 17% for prostate cancer, to 14% for corpus uteri cancer, 12% for cervix cancer, 10% for female breast cancer, 8% for ovary cancer, 5% for colon cancer, 4% for rectum and bladder cancer, 2% for stomach cancer, 1% for lung and bronchus cancer, and a "zero" survival rate for pancreas cancer for that period. The overall death rate for those afflicted by distant or disseminated cancers, after a period of five years, is 91%.<sup>1</sup>

Respondents consider this latter figure to be of particular significance herein, due to the fact that the respondents, together with thousands of other patients who have availed themselves of Laetrile or amygdalin are "terminal", namely, no conventional therapy is of any avail to prolong their lives beyond the dismal life span heretofore shown by the government's statistics, and which inescapably reflect the inadequacy and inefficacy of conventional cancer therapies. Thus, respondent Rutherford and those others who have petitioned the Courts, and who also have

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<sup>1</sup> See testimony of Dr. Marvin Schneiderman, Associate Director, National Cancer Institute, March 5, 1979, before Special Subcommittee, U. S. Senate, Edward Kennedy, Chairman; "Facts of Life and Death", U. S. Department of Health, Education and Welfare Publication No. (HRA) 74-1222; "Mortality Trends for Leading Causes of Death", U. S. Department of Health, Education, and Welfare Publication No. (HRA) 74-1853; "Ca-A Cancer Journal for Clinicians"; "Cancer Rates and Risks", 2nd Edition, U. S. Department of Health, Education, and Welfare Publication No. (NIH) 75-691.



been recognized by the legislatures of 19 states to date, believe that Laetrile offers hope as against virtually no hope whatsoever from conventional therapies.

In this connection the petitioner agency apparently believes that cancer patients should willingly and cheerfully die, rather than have Laetrile. In the Administrative Rule Making Hearing on Laetrile, held by FDA on May 2, 1977, Dr. Samuel C. Klagsbrun participated on behalf of the Agency. (Hrg. transcript, page 60, et seq.)

Dr. Klagsbrun is a psychiatrist who was instrumental in setting up an auspice for dying patients. Although a medical doctor, Dr. Klagsbrun does not treat his patients to get them well, but specializes in "helping cancer patients to die". Concerning conventional therapies for cancer, Dr. Klagsbrun stated (page 65): "the odds are slim, we know that, you are not talking to somebody who thinks it is a terrific thing that we have." Nevertheless, Dr. Klagsbrun proudly testified as to successfully discouraging cancer patients from seeking alternate therapies in Mexico, or elsewhere, and in two instances which he noted had been "successful" in convincing the terminal cancer patient to die rather than opt for an alternative therapy.

This conclusion that cancer patients should willingly die rather than seek alternate therapies lies at the heart of what is involved herein. When somebody is terminally ill from cancer, when orthodox treatments can offer nothing, then the terminal cancer patient has the inalienable right and final choice to choose between Dr. Klagsbrun's "success" in dying, and an alternate cancer therapy, involving Laetrile, after informed consent by the administering physician.

### **Petitioner Discriminates with a "Double Standard" of Safety**

The District Court, upon reviewing the voluminous record before the petitioner agency herein determined that Laetrile, or amygdalin, was "safe" and "generally recognized as safe", criteria applied in the Court's ruling that Laetrile is "grandfathered" pursuant to the applicable provisions of the Federal Food, Drug, and Cosmetic Act.

In an attempt to reverse these findings of the District Court, petitioner herein represents to this Court that somehow Laetrile is "not safe", but "toxic" (in the oral form, at least), and that therefore Laetrile does not meet the strict standards of "safety" which are a prerequisite to Food and Drug Administration approval of any anticancer drugs. (See, for example, pages 9, 14, and 46, petitioner's brief).

Not only are the District Court's findings on "safety" attacked by FDA here, but, likewise, the decision of the U. S. Court of Appeals for the Tenth Circuit, characterized by petitioner as stating that "FDA had failed, in the court's view, to advance a standard against which to measure the safety and effectiveness of Laetrile with respect to such patients . . ." (page 13).

Despite voluminous legal citations in its brief on "safety", also efficacy", it is indeed true, nevertheless, that nowhere does FDA indicate, practically and factually, what such standards might be, to be applied by this Court.

In recognition, perhaps, of the inadequacy of the record before the District Court to merit such an attack on the safety of Laetrile, petitioner's brief contains numerous references to matters not actually before the District Court, but consisting of reports in outside "medical literature". For example, at page 9 of its brief, petitioner cites several

such "reports" as to the oral Laetrile, including the alleged death of an eleven-month-old girl who is stated to have ingested amygdalin tablets. As to this alleged fatality, however, petitioner does not reveal to the Court that the hospital records underlying this particular case do not disclose that the child in question ever had amygdalin or "Laetrile" in any form!

Also cited by petitioner (page 9 of its brief) is a "dog study" wherein various dogs, previously tranquilized, were "force-fed" massive amounts of amygdalin, through tubes, the tranquilized dogs predictably succumbing to these pre-planned circumstances. At least one Court has found this so-called "study" to be of questionable validity.<sup>2</sup>

Although petitioner attempts to lump together the oral and injectible forms of Laetrile, and attacks the "safety" of this injectible form of amygdalin, once again employing "outside medical literature", the actual toxicity stated (page 9 of its brief) is limited to "A Report of Two Cases" reported in the Journal of the American Medical Association in 1977, and allegedly involved "symptoms of rash, fever, malaise, headache, and severe abdominal cramps" which disappeared upon discontinuance of Laetrile in those two cases.

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<sup>2</sup> See *In the Matter of JOSEPH HOFBAUER*, Family Court, County of Saratoga, New York, 1978, affirmed 411 N.Y.S. 2d 416 (December, 1978) and wherein the Court found "25. That petitioners produced one expert who claims that as a result of a study of 10 dogs he determined that amygdalin (Laetrile) was toxic. This court finds that that study was of questionable validity and that in fact amygdalin (Laetrile), although toxic, as are all substances, is, for the purposes of this proceeding, a non-toxic substance, the scientific evidence clearly demonstrates that on the issue of toxicity amygdalin (Laetrile) is clearly less toxic than the drugs used in conventional therapy."

Opposed to this very limited "anecdotal" report is the experience of thousands of cancer patients throughout the United States who have received and are receiving Laetrile with complete safety.<sup>3</sup>

Concerning the criterion of "safety" urged by petitioner to be applied by this Court as to the instant cause, it is stated (page 31 of its brief):

"A drug is 'safe', within the meaning of the Act, if the benefits expected to be achieved through its administration outweigh the costs of risks incurred."

Presumably, therefore, FDA has applied and applies these standards of "safety" in numerous instances whereby anticancer drugs have been approved by the Agency for use by physicians, and for administration to cancer patients. However, in the instance at hand, and whether or not due to its implacable opposition to Laetrile over the years, FDA has not even-handedly and non-discriminately applied to Laetrile the same standards by which it has measured other anticancer drugs for "safety" and "efficacy".

Whereas for quite minor reasons FDA attacks herein the "safety" of Laetrile, even attempting to reverse the findings of the District Court on such subject, nevertheless, by applying a "double-standard" of such criterion, many very toxic, grossly dangerous, even lethal and fatal drugs have been approved in the name of "safety" by the Agency.

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<sup>3</sup> For example, Dr. Bruce Halstead, a California physician, biotoxicologist, academician, and researcher, has noted that as to amygdalin or "Laetrile", "Upwards of 75,000 people are taking somewhere in the vicinity of an excess of one million grams of laetrile a month in the United States", with safety. Dr. Halstead further described the toxicity of various conventional anticancer drugs as being "practically at war gas level". (See aforesaid case of *In re HOFBAUER*.)

To designate these circumstances, respondents consider it only proper that they should make reference to authoritative medical literature, in particular concerning FDA-approved "safety" standards as to other anticancer drugs. In this regard, respondents refer to the publication "Physicians' Desk Reference", 33rd Edition, 1979.<sup>4</sup>

**CYTOXAN** (Mead Johnson & Co.) A dangerous drug which can cause death. This FDA-approved "anticancer" drug actually can also cause cancer, namely secondary malignancies. According to the FDA-approved "safety" data: "the possibility of secondary malignancy, based on available data, should be considered in any benefit-to-risk assessment for the use of the drug." In addition to causing cancer and death, numerous side-effects can occur from this drug, including destruction of immune systems, leukopenia, hemorrhage, gonadal suppression, resulting in amenorrhea or azoospermia, possibly "irreversible". The drug is not represented to be cancer-curative. See Exhibit A herein, page 18.

**ADRIAMYCIN** (Adria Laboratories Inc.) The FDA-approved data on "safety" states that special attention

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<sup>4</sup> This is a standard reference work for doctors, wherein each product description has been prepared by the manufacturer, and edited and approved by the manufacturer's medical department, medical director, and/or medical consultant. Any products described in such publication which have official package circulars must be in full compliance with Food and Drug Administration regulations pertaining to labeling for prescription drugs, and any "indications, effects, dosages, routes, methods, frequency and duration of administration and any relevant warnings, hazards, contraindications, side effects, and precautions" must be in the "same language and emphasis" as the FDA-approved labeling for the product. (See Exhibit A herein, pages 1 and 2)

"must be given to the cardiac toxicity" exhibited by this drug. Such labeling data further states that "Congestive heart failure and/or cardiomyopathy may be encountered several weeks after discontinuation" of therapy with this drug, and that cardiac failure is often "not favorably affected by presently known medical or physical therapy for cardiac support." According to such labeling, there is a "high incidence of bone marrow depression" and administration of the drug "may result in superinfection or hemorrhage." Numerous severe and body-damaging adverse reactions are also listed in the approved labeling, including acute nausea and vomiting, phlebosclerosis, severe cellulitis, vesication and tissue necrosis (death), fever, chills and anaphylaxis. The drug is not stated to be cancer-curative. (See Exhibit A herein, page 3).

**ADRUCIL** (Adria Laboratories Inc.) According to the manufacturer's FDA-approved "safety" data, this is a "highly toxic drug with a narrow margin of safety." It is further stated that "severe hematologic toxicity, gastrointestinal hemorrhage, and even death may result" from use of this drug, despite "meticulous selection of patients and careful adjustment of dosage." "Myelosuppression" (bone marrow suppression, particularly spinal) "almost uniformly accompanies a course of adequate therapy" with this drug, according to the aforesaid approved FDA labeling. Other and severe dangerous effects are also described in such labeling. The alleged benefits are stated to be "palliative" (i.e., "affecting relief, not cure".<sup>5</sup>) (See Exhibit A herein, page 4).

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<sup>5</sup> Dorland's Illustrated Medical Dictionary, 25th Edition.



*BICNU* (Bristol Laboratories, Division of Bristol Myers Co.) According to the FDA-approved "safety" data for this drug, "delayed bone marrow toxicity is the major toxicity". Other and serious side effects and adverse reactions are also listed. Additionally, the drug causes cancer, the FDA-approved labeling stating "BICNU is carcinogenic in rats and mice, producing a marked increase in tumor incidence in doses approximating those employed clinically." Alleged "benefits" are stated to be "palliative". (See Exhibit A herein, page 6.)

*CeeNU* (Bristol Laboratories, Division of Bristol Myers Co.) The FDA-approved "safety information" for this drug lists as the "major toxicity" delayed bone marrow suppression. The official labeling also lists cumulative myelosuppression as an effect which can result from this drug. It is also stated: "Neurological reactions such as disorientation, lethargy, ataxia" (failure of muscular coordination) "and dysarthria" (impaired speech) "have been noted in some patients receiving CeeNU." Alleged "benefits" are stated to be "palliative". (See Exhibit A herein, page 10.)

*DTIC* (Dome Division, Miles Laboratories, Inc.) The "safety" data approved by FDA for this drug states: "Leukopenia and thrombocytopenia may be severe enough to cause death." According to FDA-approved labeling, more than 90% of patients are affected with the initial few doses as to anorexia, nausea and vomiting, among other things. The drug is not stated to be cancer-curative. (See Exhibit A herein, page 13.)

*MUTAMYCIN* (Bristol Laboratories, Division of Bristol Myers Co.) The FDA-approved "safety" data for this product states: "Bone marrow suppression, notably throm-

bocytopenia and leukopenia, which may contribute to overwhelming infections in an already compromised patient, is the most common and severe of the toxic effects of Mutamycin." Elsewhere in the FDA-approved labeling, it is stated that such bone marrow toxicity occurred in 64.4% of a group of patients tested. It is also stated that: "About 25% of the leukopenic or thrombocytopenic episodes did not recover" (i.e., died). Among the other "undesirable side effects" listed in the FDA-approved labeling are "headache, blurring of vision, confusion, drowsiness, syncope" (i.e., temporary suspension of consciousness), "edema, thrombophlebitis, hematemesis, diarrhea, and pain." In addition, this "anti-cancer" drug causes cancer, with an increase of 50% to 100% in cancer tumors, the official FDA-approved labeling stating: "Mutamycin has been found to be carcinogenic in rats and mice. At doses approximating the recommended clinical dose in man, it produces a greater than 100 percent increase in tumor incidence in male Sprague-Dawley rats, and a greater than 50 percent increase in tumor incidence in female Swiss mice." This drug is not alleged to be cancer-curative. (See Exhibit A herein, page 11.)

*MATULANE* (Roche Laboratories.) In addition to numerous adverse reactions which are caused by this drug, it is also cancer-causing. According to the FDA-approved "safety" data, leukemia, among other things, has resulted from "Matulane therapy". Animal tests reveal other forms of cancer caused by administration of the drug, according to the approved labeling. (See Exhibit A herein, page 23.)

*MITHRACIN* (Manufactured by Pfizer Laboratories for the Dome Division, Miles Laboratories, Inc.) The FDA-approved "safety" data for this product states: "Severe

thrombocytopenia, a hemorrhagic tendency and even death may result from the use of Mithracin." It is further stated that a detailed analysis of the clinical data in 1,160 patients treated with the drug "indicates that the hemorrhagic syndrome is dose related." The manufacturer also notes, with FDA approval, that with recommended "doses of 30 meg/kg/day or less for 10 or fewer doses" there is an "associated drug-related mortality rate of 1.6%" (16 patients per 1,000 receiving the drug are killed by the drug, in other words, not their cancer). The FDA-approved death rate from this drug rises to 5.7% (or 57 per 1,000) however, with a higher dosage of "Mithracin" noted in said approved labeling. The approved labeling also designates a veritable host of other dangerous side effects. The drug is not stated to be cancer-curative. (See Exhibit A herein, page 14.)

*FUDR* (Hoffman LaRoche, Inc.) According to the FDA-approved official labeling in effect as of August 1, 1978: "Severe hematological toxicity, gastro-intestinal hemorrhage and even death may result from the use of *FUDR* despite meticulous selection of patients and careful adjustment of dosage . . . fatalities may be encountered occasionally even in patients in relatively good condition." Numerous other adverse effects of this dangerous drug include functional gastrointestinal, mucosal gastrointestinal, hematologic, dermatologic, miscellaneous clinical reactions, laboratory abnormalities and procedural complications of regional arterial infusion, nausea, vomiting, diarrhea, enteritis, stomatitis, and localized erythema, anemia, leukopenia, and others. Alleged "benefits" are stated to be "palliative". (See Exhibit A herein, page 22.)

*FLUOROURACIL* (Hoffman LaRoche, Inc.) The official FDA-approved "safety" labeling in effect as of August 1, 1978 states: "Severe hematological toxicity, gastrointestinal hemorrhage and even death may result from the use of Fluorouracil despite meticulous selection of patients and careful adjustment of dosage." Numerous other adverse and dangerous reactions and side effects are also listed in such official labeling. Alleged "benefits" are stated to be "palliative", only. (See Exhibit A herein, page 20.)

*METHOTREXATE* (Lederle Laboratories.) The "safety" data contained in the FDA-approved labeling for this product states that "sudden death has been reported from use of Methotrexate." It is also stated that the drug "may produce marked depression of bone marrow, anemia, leukopenia, thrombocytopenia and bleeding", it may be "Hepatotoxic" (liver damaging) and cause "liver atrophy, necrosis" (death), "cirrhosis, fatty changes, and periportal fibrosis". It is also stated that this drug, approved by FDA for its "safety", may have an "immunosuppressive action" (i.e., destroying the immune systems of the body). Listed as "common adverse reactions" are included ulcerative stomatitis, leukopenia, nausea and abdominal distress, malaise, decreased resistance to infection, depigmentation, alopecia, hemorrhage from various sites, vomiting, diarrhea, gastrointestinal ulceration and bleeding, renal (kidney) failure, infertility, abortion, severe nephropathy (kidney disease), blurred vision, paresis (paralysis) and convulsions, ataxia, dementia, precipitating diabetes, osteoporotic effects (calcium leached from the bones), abnormal tissue cell changes, and others. The drug is not stated to be cancer-curative. (See Exhibit A herein, page 16.)

**BLENOXANE** (Bristol Laboratories, Division of Bristol Myers Co.) The FDA-approved "safety" data for this product states: "Pulmonary fibrosis" (i.e., progressive fibrous degeneration of the lung) "is the most severe toxicity associated with Blenoxane." It is further stated that in approximately 1% of patients treated with Blenoxane, "the nonspecific pneumonitis induced by Blenoxane progresses to pulmonary fibrosis, and death. Although this is age and dose related, the toxicity is unpredictable." The same FDA-approved mortality data is repeated elsewhere: "Approximately 1% of patients treated have died of pulmonary fibrosis." Numerous other dangerous and harmful effects of this drug are also listed in the FDA-approved representations. The drug is not stated to be cancer-curative. (See Exhibit A herein, page 8.)

The foregoing illustrate the nature and type of anti-cancer drugs approved by the petitioner agency for "safety" and "efficacy". Are any of these drugs curative of the cancer conditions for which they are offered? If so, the FDA-approved labeling is devoid of any such claims or representations. And, does a mere "palliative" or "relieving" effect, temporary at best, of a drug justify imposing upon an innocent cancer patient body-destroying, even death-dealing effects from drugs which may, in and of themselves, cause cancer, adding to the plight of the already diseased patient? Respondents respectfully urge that this Court shall apply the rule of common sense to the criteria urged upon the Court as to Laetrile, and concerning which the same is totally "non-toxic", and "safe", if only judged by the standards heretofore applied by FDA as to approved drugs now available and employed by doctors for their cancer patients.

Small wonder that thousands of cancer patients throughout the United States have opted to avoid the deadly effects of FDA-approved cancer drugs in favor of Laetrile, and small wonder that the legislatures of 19 states have perceived the need for cancer patients to have made available to them Laetrile, or amygdalin, in lieu of the ineffective and deadly drugs now available through orthodox medical channels.

### **"Consensus of Ignorance" No Substitute for Scientific Expertise**

In attempting to reverse the District Court's finding that Laetrile, or amygdalin, was "generally recognized as safe" on October 9, 1962 (a criterion for holding that Laetrile is "grandfathered", and therefore may be distributed without interference by FDA), petitioner, at page 46 of its brief, states that in 1962 there was no such "general recognition of safety", because "Laetrile was not generally known at all to the community of medical experts".

In the first place, there is no "community" of scientists or doctors, any more than there is a "community" of lawyers, teachers, butchers, or other professional persons, speaking in "unison", so to speak, on a given subject.

Whatever the case, no provision whatsoever of the Federal Food, Drug, and Cosmetic Act provides that merely because "experts" know nothing of a substance, that this obviates "general recognition" by those who are actually qualified to express an opinion.

Section 201 (p) of the Federal Food, Drug, and Cosmetic Act, as in effect on October 9, 1962, designated a criterion of "general recognition of safety" by "experts



qualified by scientific training and *experience*" to evaluate safety of a substance. (Emphasis supplied) It is respectfully submitted that "ignorance" of a substance cannot under any circumstances be held to constitute the requisite "experience" mandated by the statute, and that, therefore, only an expert having real knowledge of Laetrile would be qualified to express an opinion concerning its safety. Conversely, the opinion of those "ignorant" of Laetrile is of no value whatsoever.

#### **Laetrile — No Issue as to Its Chemical Identity**

In its attempt to upset and reverse the findings of the U. S. District Court concerning the "grandfather clause" of the Federal Food, Drug and Cosmetic Act, as applied to "Laetrile", petitioner attempts to delineate to this Court (page 41, et seq.) that somehow there is no identifiable entity which could be termed "Laetrile". This is entirely contrary to fact, even as noted in the Commissioner's Decision on Status" (42 Federal Register, No. 151, Page 39768, et seq.), wherein, the FDA commissioner noted that the Merck Index, 9th Edition, designates "laetrile" as "a term used interchangeably with 'Laetrile', 'amygdalin', 'nitriloside', and 'vitamin B-17'." The record also clearly shows that the chemical identity of "amygdalin" is not new, but has been known to science since at least 1845.

#### **No "Efficacy" Requirement — 1962 Grandfather Clause**

After an exhaustive and voluminous review of the entire record, the U. S. District Court found that "Laetrile", or amygdalin, was "grandfathered" as of October 9, 1962, pursuant to the applicable provisions of the Federal Food, Drug and Cosmetic Act, the principal criterion applied in

this regard being that it was, at such time, "generally recognized as safe".

Petitioner would have the Court believe, however, that, although the statute in question does not require "efficacy" as one of the criteria of this "grandfather" provision, that nevertheless this criterion must be applied to Laetrile, and it is therefore barred from distribution.

However, the statutory provisions aforesaid are very clear. If Congress had intended that "efficacy" should be added to "safety" as a necessary component of the 1962 "grandfather clause", it could readily have done so. But, Congress did not. In fact, the "Kefauver Amendments" of 1962, enacted at the same time, *added* an "efficacy provision to the "new drug" definition to apply *after* October 9, 1962. (See Sec. 201 (p) of the statute as presently in force).

Concerning these circumstances, the District Court ruled (See Memorandum opinion and order, April 8, 1977, App. page 53):

"... FDA contends that if laetrile were marketed prior to 1962 it must still be shown to have been 'effective' as well as 'safe' if employed in the treatment of 'a life-threatening disease.' *Durovic v. Richardson*, 479 F.2d 242 (7th Cir. 1973). The Supreme Court in *Weinberger v. Hynson, supra*, stated that 'the 1962 amendments (of the Food, Drug and Cosmetic Act) for the first time gave FDA power to scrutinize and evaluate drugs for effectiveness as well as safety.' at 630. In any event, the case relied upon by FDA is clearly distinguishable from the case at bar. In *Durovic v. Richardson, supra*, the Court held that '(a)ny delay in the institution of effective therapy (e.g., radiation, surgery, effective chemotherapy) caused by the use of an ineffective drug allows the disease to progress

beyond control. Delay means almost certain death.' Significantly, in the present case plaintiff class is comprised of persons already determined to be terminally ill. Adopting FDA's rationale would mean that an individual suffering from a life-threatening disease for which there exists no known effective treatment would not lawfully be entitled to any treatment at all since no drug could be deemed 'generally recognized as effective' in such a situation."

### **FDA Ignores Value of Laetrile**

Whatever technical statutory provisions might apply to Laetrile, it is still worthy of note that it has proven of value to the many thousands of cancer patients and physicians who have employed it in this Country, and elsewhere. Petitioner chooses to ignore such value repeatedly proclaiming Laetrile to be "fraudulent", "useless", "of no value", and the like.

For example, FDA ignores herein a ten-year clinical study of Laetrile conducted by three European scientists (Ettore Gnidetti, Christian Deckers, and Benedetto Rossi), the results of which were available to the scientific world as early as 1966, per report of such clinical investigation presented to the Ninth International Cancer Congress, as conducted under the auspices of the International Union Against Cancer. By way of background, this organization includes within its ranks the pre-eminent cancer scientists of the World, including various prestigious orthodox oncologists of the United States.

These European scientists concluded that Laetrile "appears to possess not only a palliative effectiveness, but also a specific and direct action against neoplastic process, peculiarly by local administration without side reactions." 150 cases of "terminal human cancers" were the subject of the clinical investigation, and, as to overall results, the

scientists stated: "We have noticed that the 50% of all cases in treatment showed an objective improvement, proved by many laboratory reports, by x-ray films and by a gain in weight." It was further stated: "We can state that the drug . . . is a suitable one, whether for its therapeutic effectiveness or on account of its extremely low toxicity." (See Exhibit B herein).

Numerous other instances of the value of Laetrile could be cited, also ignored herein by FDA.

In this regard, respondent Rutherford notes that he himself attributes his very life and present good health to Laetrile, a substance which FDA sought to ban him from obtaining, and only made available for his cancerous condition by intervention of the District Court in this proceeding.

### **FDA Attempts to Destroy State Laws by Bureaucratic Fiat**

Throughout its brief Petitioner argues that Laetrile should be denied to everyone because it is a "fraudulent drug", and its mere use constitutes a "fraud".

At Page 68 of its brief, petitioner urges that terminally ill patients or members of the public generally should be denied Laetrile, because they do not have a "Constitutional right of access" to it. And, states FDA further, the right to have Laetrile should be denied "by compelling governmental interests in protecting the public health, reinforced by a legitimate interest in preventing fraud." This ignores, and by silence implies the nonexistence of a very important circumstance, namely the passage by *nineteen States* thus far of laws specifically permitting and approving the use of Laetrile for their citizens, and wherein there is

actually recognition of a "compelling governmental interest" in making available Laetrile in those States.<sup>6</sup>

The nineteen States are: Alaska; Arizona; Delaware; Florida; Idaho; Illinois; Indiana; Kansas; Louisiana; Maryland; Nevada; New Hampshire; New Jersey; North Dakota; Oklahoma; Oregon; South Dakota; Texas; and Washington.<sup>7</sup>

Certain State laws, such as enacted in Illinois, include provisions for "informed consent" to be rendered by the treating physician, and acknowledged by the cancer patient, before treatment with Laetrile commences. In the main these statutes properly equate "Laetrile" and "Amygdalin". All of these State laws were enacted only after extensive hearings, research, and debate. Laetrile legislation is presently pending in various other States. South Dakota is the most recent state to approve Laetrile, its law having been enacted March 16, 1979.

Petitioner's brief contains *not one* word as to these laws!

<sup>6</sup> Laetrile is, of course, also employed and administered by physicians in various States which have not yet enacted formal legislation.

<sup>7</sup> *Alaska* (See Alaska Statutes 08.64.367); *Arizona* (See A.R.S. 36-2451); *Delaware* (See Del. Code Ann. 16 Section 4901); *Florida* (See F.S.A. 458.24); *Idaho* (See Idaho Code 18-7301A); *Illinois* (See S.H.A. 56½, Section 1801); *Indiana* (See Burns Ind. St. Ann. 16-8-8-1); *Kansas* (See S.B. 505 May 8, 1978); *Louisiana* (See L.S.A.—R.S. 40:676); *Maryland* (See Ann. Code of MD, Art 43 Sec. 133 ch 809); *Nevada* (See Nev. Rev. St. 630.303); *New Hampshire* (See R.S.A. 329:30); *New Jersey* (See N.J.S.A. 24:6F-1); *North Dakota* (See H.B. 1214 eff. July 1, 1979); *Oklahoma* (See 63 Okl. St. Ann. Sec. 2-313); *Oregon* (See Oregon Rev. St. 689.885); *South Dakota* (Bill Number 1287 signed 3/16/79 eff. 7-1-79); *Texas* (See Vernon's Ann. Civ. St. 71 art. 4476-5a.); *Washington* (See R.C.W.A. 70.54.130).

### Laetrile Denied to the States

Despite the widespread, definitive State Laetrile legislation noted above, FDA seeks, nevertheless, by banning any interstate distribution of Laetrile, *per se*, or even any substance containing it and from which it may be extracted, to thwart and render of no effect the laws of any state making available Laetrile to its citizens.<sup>8</sup>

Rather obviously, without Laetrile being available, the cancer patient and his Doctor, even though under sanction of an appropriate State law, are barred from its use if none is available and FDA governmental dictates are employed to insure such prohibition.

In an obvious attempt to mute and avoid these clear implications, petitioner's brief states (page 45): "no provision of Federal law directly prohibits personal use or affects any supply that has neither been imported nor had any connection with interstate commerce."

This covert and carefully chosen language ignores the breadth and scope of the commerce clause of the U. S. Constitution, even only as developed since *Wickard v. Filburn*, 317 U. S. 11 (1942), legalities followed in the food and drug area.

In *Palmer v. U. S.*, 340 F.2d 48 (5th Cir. 1964), the Court held for example, that the shipment of the active ingredient of a drug (in the case at bar, "amygdalin") is

<sup>8</sup> Amygdalin or Laetrile occurs naturally in approximately twelve-hundred different fruits, vegetables, grains and seeds, including apricot kernels, strawberries, macadamia nuts, lima beans, barley, rye, apple seeds, peach kernels and cherry pits. See *Millet, Pit and Seed Co. v. U. S.*, 436 F. Supp. 84 (E.D. Tenn. 1977). The best food substance for extraction of its Laetrile component is apricot kernels, the major U. S. source of which is the State of California.



the equivalent of shipping the drug. Cf. *U. S. v. 40 Cases More or Less, of Pinocchio Brand 75% Corn, Peanut Oil Blended with 25% Pure Olive Oil*, 289 F.2d 343 (2nd Cir. 1961); *U. S. v. 39 Cases, More or Less, Mich. Brand Korleen Tablets*, 192 F. Supp. 51 (N.D. Mich. 1961).

Thus, even if one in a State having Laetrile-enabling legislation desired to import through interstate channels an amygdalin containing substance from which to extract Laetrile, the petitioner agency could, under the circumstances it urges herein, and would, ban such importation.

That such bureaucratic procedure would effectually thwart, and render of no effect, the Laetrile laws of any State cannot be doubted. Of interest in this connection is the following excerpt from *Laetrile: The Battle Moves Into The Courtroom*, 65 A.B.A. Journal 224, 226 (February, 1979):

"But even if Laetrile cannot be imported or moved in interstate commerce, why can't it be used legally if it is grown and processed locally? First, many states lack either the facilities for processing the drug or the climate for producing it. Alaska, for example, was the first state to legalize its use, and the drug might be in use more commonly there if a legislature could cause apricot trees to grow around the Arctic Circle."

#### **FDA Opposition to Laetrile Not Based Upon Science**

From merely reading petitioner's brief herein, one would suppose that the FDA attitude toward Laetrile is scientifically based upon the "rule-making" proceeding which occurred in 1977, upon mandate of the District Court and the U. S. Court of Appeals for the Tenth Circuit.

However, this is not the case, the FDA opposition to Laetrile having long predated any such proceeding.

For example, during a 1974 question-answer session, when former FDA Commissioner Schmidt was asked by reporters whether FDA had tested or will test Laetrile in view of the fact that at least 5,000 persons in the U. S. believe it has helped them, the Commissioner "in a voice heavily laced with sarcasm" replied: "The fact that 5,000 people—or 10,000 people—or 15,000 people believe something—even if they are physicians—does not prove anything."<sup>9</sup>

Even as of 1979 FDA has still not tested Laetrile.

The implacable FDA opposition to Laetrile was duly noted by the District Court as the within cause was commenced in 1975, when, respondent Rutherford's Laetrile having been seized by petitioner, he sought Court intervention. At that time, FDA had conducted no administrative proceeding whatsoever to determine the legal status of Laetrile.

FDA appealed the 1975 District Court decision aforesaid to the U. S. Court of Appeals for the Tenth Circuit, which Court, on October 12, 1976 (App. page 31) upheld the Lower Court, its opinion stating that Laetrile "is not a new drug merely because they" (i.e. FDA) "say it is." The Court ordered an administrative review by FDA, which in turn led to the 1977 rulemaking proceeding in question. In view of the previous bias and prejudice of FDA against Laetrile, the ruling of the Commissioner referred to in petitioner's brief herein was eminently predictable.

Nor has FDA's opposition to Laetrile abated since injunctions were ordered by the District Court and the U. S. Court of Appeals for the Tenth Circuit subsequent

<sup>9</sup> San Jose, California "Mercury", March 25, 1974.

to such rulemaking proceeding. And, although proclaiming the "need for regulation" of Laetrile, allegedly to prevent "fraud" and other misdeeds, petitioner has not even deigned to carry out the most recent rulings of the U. S. Court of Appeals (582 F. 2d 1234), stating:

"We are confident that the FDA with all due dispatch will promulgate regulations within the above limitations and as if the drug was found by the Commission to be 'safe' and 'effective' for the limited group of persons here considered."

**Respondent Rutherford, et al. — No Means or Resources To Follow "New Drug" Procedures**

The District Court held, and properly so, that Laetrile, or amygdalin, is "grandfathered" pursuant to the applicable provisions of the Federal Food, Drug and Cosmetic Act. However, FDA combats this ruling herein, urging to the Court that only through processing of a "new drug application" to be presented to the Agency, can Laetrile be validated for interstate distribution to cancer patients, or anyone else, for that matter.

Although the filing of a "new drug application" seems simple, on the face of it, in all practicality, to follow such procedure for an individual such as Respondent Rutherford, would in effect sentence him and many others to death, due to the fact that neither he nor thousands of other cancer patients would individually have the means or resources with which to pursue the complicated and drawn-out procedures involved therein.<sup>10</sup>

<sup>10</sup> One industry source has estimated that the average new drug proceeding requires ten or more years in time, and an expenditure of approximately \$12,000,000.00 per drug, on an average, before approval thereof, with only a relative handful of drugs being approved each year by FDA for the entire pharmaceutical industry.

In this regard, the District Court made appropriate findings at the very outset of the cause at bar, stating in its Findings of Fact and Conclusions of Law issued August 14, 1975 the following (App. page 24):

"In this connection the Court finds that laetrile has been in use for a number of years in Mexico and other nations around the world; that the FDA has by its regulations made it impossible for the common man to have an application processed through FDA so that said agency would either approve or disapprove the drug known as laetrile. The Court finds that Congress intended by 21 U.S.C. Sec. 355 that the FDA would on its own initiative and in good faith approve or disapprove the use of laetrile, thereby allowing the courts jurisdiction of the subject matter.

"The Court finds that the FDA has abdicated its duty to make a clear determination of whether the drug laetrile should or should not be placed in commerce though the drug has been in use for many years and thousands of persons have been treated with it.

"The Court finds from the record, testimony and exhibits that laetrile is not lethal in any sense of the word. It is not harmful to the human body and when used in proper amounts under proper control and supervision can effect relief from cancer disease to the satisfaction of many who are privileged to use the same."

And (App. page 27):

"The Court finds that the plaintiff Rutherford and those similarly situated are wholly without means or resources to comply with the provisions of 21 U.S.C. Sec. 355(b) and that for the plaintiff Rutherford and those similarly situated to be denied the freedom of choice for treatment by laetrile to alleviate or cure

their cancer, was and is a deprivation of life, liberty or property without due process of law guaranteed by the Fifth Amendment to the Constitution of the United States."

### **Important Constitutional Rights Involved**

The record below fails to establish evidence of a "compelling interest" on the part of petitioner FDA sufficient to prevail over respondents' constitutionally guaranteed right of privacy in their choice of Laetrile treatment.

This Court has consistently held that when certain "fundamental rights" are involved, regulation may be justified only by a "compelling state interest," and further, that legislative enactments "must be narrowly drawn to express the legitimate state interests at stake." *Roe v. Wade*, 410 U.S. 113, at 155.

Petitioner's asserted interests in regulation of Laetrile for use by respondents do not meet the strict test required by this Court. As against the terminally ill cancer patient's right to choose a nontoxic substance for his own health care, petitioner FDA's arguments are not compelling by any standard.

First, petitioners claim that without regulation, consumers of Laetrile will be "harmed" by the resulting postponement of other approved supposedly "effective" methods of cancer treatment. The real fear, apparently, is that cancer patients will unwittingly select Laetrile over orthodoxy. Yet the record below discloses that the vast majority of Laetrile patients first underwent the relevant conventional treatments. 438 F. Supp. 1287, at 1296, n. 18 (1977). This fact is acknowledged in petitioner FDA's own report on Laetrile. (R. 507, R. 313 at J 242).

With respect to the argument that the choice of Laetrile may be *unwitting* or *uninformed*, the Federation would

point out that the affidavit procedure establishing respondents' class requires an intelligent, informed choice.

Many cancer victims have investigated and evaluated the merits of surgery, radiation therapy or chemotherapy with the aid of competent medical advice and have still made the highly personal choice to try Laetrile; the benefits from orthodox treatment are not considered sufficient, at the very least, to justify the risks which include disfigurement, debilitation, and accelerated death, and even additional cancer caused by the treatment. Respondents are a subgroup of the class of all cancer patients. They alone have been advised that their condition is hopeless, and terminal. As a first or last result, they seek Laetrile. As to them, petitioner can have no interest in regulation.

Petitioner FDA further attacks the credibility of "cures" reported to have been effectuated by Laetrile. The Federation answers here that it has no interest in the promotion of Laetrile as a "cure." This depends upon the individual case. Still, petitioner FDA argues that in various instances, the person involved may never even have had cancer. This claim is specious and unsupported in the record below; it is wholly irrelevant and hardly reassuring to respondents, who unfortunately *do* have cancer. It can carry no weight with respondent Glen Rutherford, for example, whose proposed surgical colostomy would *unalterably* have lessened the quality of his life, irrespective of the ultimate outcome of his illness. See, 438 F. Supp. 1287, 1299, n. 25 (1977).

The right of the patient is of such fundamental nature its free exercise may be impinged upon or forbidden only by such Governmental interest as may be a "compelling interest."



The "fundamental" nature of this right derives from its source. It flows from the very nature of man. Justice Brandeis in *Olmstead v. United States*, 277 U.S. 438, 478 [72 L.Ed. 944, 956, 48 S.Ct. 564, 572 (1928)] stated:

"The makers of our Constitution undertook to secure conditions favorable to the pursuit of happiness. They recognized the significance of man's spiritual nature, of his feelings and of his intellect. They knew that only a part of the pain, pleasure and satisfactions of life are to be found in material things. They sought to protect Americans in their beliefs, their thoughts, their emotions and their sensations. *They conferred, as against the government, the right to be let alone—the most comprehensive of rights and the right most valued by civilized men.* To protect that right, every unjustifiable intrusion by the government upon the privacy of the individual, whatever the means employed, must be deemed a violation. . . ." (Italics added.)

Judge Cardozo in *Schloendorff v. Society of New York Hospital*, 211 N.Y. 125 [105 N.E. 92, at page 93] stated:

"Every human being of adult years and sound mind has a right to determine what shall be done with his own body; . . ."

The right to control one's own body is not restricted to the wise; it includes the "foolish" refusal of medical treatment. Nor is this right limited in its recognition to any single segment of the political, economic, or social thought spectrum.

In commenting upon Justice Brandeis' most valued of rights, the right to be left alone, Chief Justice Burger, in his now well-known dissent in *Application of President & Directors of Georgetown Col.*, 331 F.2d 1010, at page 1017, stated:

"Nothing in this utterance suggests that Justice Brandeis thought an individual possessed these rights only as to *sensible* beliefs, *valid* thoughts, *reasonable* emotions, or *well-founded* sensations. I suggest he intended to include a great many foolish, unreasonable and even absurd ideas which do not conform, such as refusing medical treatment even at great risk."

Without specific reference to a constitutional basis, the right to choose what may be even a suicidal medical course has been upheld. In *Erickson v. Dilgard*, 44 Misc. 2d 27 [252 N.Y.S.2d 705, 706] a New York court sustained the unwilling Jehovah's Witness' objection to a needed blood transfusion despite risk of death. The court there said at page 706:

"... it is the individual who is the subject of a medical decision who has the final say and that this must necessarily be so in a system of government which gives the greatest possible protection to the individual in the furtherance of his own desires."

In *Whalen v. Roe*, 429 U.S. 589, this Court considered the New York statutory requirements with respect to prescriptions for "dangerous, legitimate" drugs. The requirement in question was that of notification. The Court balanced the invasion of the zone of privacy against the public's right involved and concluded that with respect to the particular type of drugs involved the statutes were a reasonable exercise of the state's broad police power. In so holding the Court discussed the right of an individual to choice of treatment saying:

"Nor can it be said that any individual has been deprived of the right to decide independently, with the advice of his physician, to acquire and to use needed medication. . . . Within dosage limits which appellees

do not challenge, the decision to prescribe, or to use, is left entirely to the physician and the patient." (Whalen v. Roe, *supra*, 429 U.S. 589, 603 [51 L.Ed.2d 64, 75-76, 97 S.Ct. 869, 878].)

This Court has held that "a right of personal privacy, or a guarantee of certain areas or zones of privacy, does exist under the Constitution" (*Roe v. Wade*, 410 U.S. 113, 152, 35 L.Ed.2d 147, 176).

While only personal rights that may be deemed "fundamental" or "implicit in the concept of ordered liberty" are included in this guarantee of personal privacy (410 U.S. 113, 152, 35 L.Ed.2d 147, 176), in his concurring opinion in the *Roe* case, Justice Douglas recognized that the "freedom to care for one's health and person" does come within the purview of the right to privacy (410 U.S. 179, 213, 35 L.Ed.2d 147, 188). Justice Douglas continued:

"It is one thing for a patient to agree that her physician may consult with another physician about her case. It is quite a different matter for the State compulsorily to impose on that physician-patient relationship another layer or, as in this case, still a third layer of physicians. The right of privacy—the right to care for one's health and person and to seek out a physician of one's own choice protected by the Fourteenth Amendment—becomes only a matter of theory, not a reality, when a multiple-physician-approval system is mandated by the State.

\* \* \*

"The good-faith decision of the patient's chosen physician is overridden and the final decision passed on to others in whose selection the patient has no part. This is a total destruction of the right of privacy between physician and patient and the intimacy of relation which that entails." (*Roe v. Wade*, 410 U.S. 113, 219, 35 L.Ed.2d 191, 192).

In *Matter of Quinlan* (355 A.2d 647, cert. den. 429 U.S. 922, 1976), the Supreme Court of the State of New Jersey held in a declaratory judgment proceeding that the parent and guardian of an incompetent woman could assert on her behalf her constitutional right to privacy. The Court further held that its decision need not be controlled by the consensus of opinion of physicians who were qualified experts, namely, that withdrawal of the support of a respirator would not conform to standard medical practices and would result in Karen Quinlan's death soon thereafter (355 A.2d 647, 669). The decision on whether or not to remove the respirator properly rested with Karen's parents and attending physicians.

#### Individual Rights Recognized by Court Below

In its decision rendered in December, 1977 (438 F. Supp. 1287), the U. S. District Court applied the foregoing principles enunciated by this Court, and by other Courts, recognizing the important Constitutional rights enjoyed by respondents.

The opinion states:

"Unintentionally FDA has wrought needless hardship and expense to countless individuals required to travel to Mexico or Germany in order to utilize Laetrile. If it were more readily available in this country, perhaps many patients currently obtaining the treatment abroad could be persuaded to remain under their doctor's care here and use the substance in conjunction with conventional treatments.

"The final consequences are ultimately borne by those whose bodies are the battleground on which cancer's war is waged. Many perceive the drug's acquisition as a life and death matter, and are understandably frustrated and enraged over attempts by their own govern-

ment to deny them the right to decide for themselves questions of such a personal and grave nature."

And:

"When certain 'fundamental rights' are invoked, such as the right of privacy involved herein, regulation may be justified only by a 'compelling state interest,' and legislative enactments 'must be narrowly drawn to express only the legitimate state interests at stake.' *Roe v. Wade, supra* at 155. By denying the right to use a nontoxic substance in connection with one's own personal health-care, FDA has offended the constitutional right of privacy.

"The court's decision in this case in no way portends the return of the traveling snake oil salesman. As emphasized earlier, the right to use a harmless, unproven remedy is quite distinct from any alleged right to promote such. FDA is fully empowered under statutory provisions to combat false or fraudulent advertising of ineffectual or unproven drugs. See the Food, Drug and Cosmetic Act, Misbranded Drugs and Devices, 21 U.S.C. § 352 (1976); and the Federal Trade Commission Act, Dissemination of False Advertisements, 15 U.S.C. § 52 (1975)."

### **FDA Reaches Back to the Middle Ages To Ban Laetrile**

In an effort to buttress its manifestly unsound legal and Constitutional position herein (presumably premised upon the Federal Food, Drug, and Cosmetic Act, enacted in 1938), the petitioner agency, presents to the Court in "Appendix A" to its brief, an anonymously-authored monograph entitled "History of Drug Regulation", designed to convince the Court that Laetrile is now, and has for centuries, been illegal "quackery" and almost "witchcraft", so to speak. In so doing, FDA reaches back to

statutes enacted as long ago as the year 1266, almost 700 years before enactment of the Act under consideration here.

This constitutes an ambitious, if historically inaccurate, project with regard to the subject matter actually before the Court, and the Federation deems it only proper that brief comment should be rendered concerning the same.

It is the overall import of "Appendix A" aforesaid that, without the statutory regulation supposedly invoked from time to time over the past some 700 years, mankind would have been deprived of the bureaucratic protection so necessary for health and welfare.

However, totally omitted from "Appendix A" are the numerous instances wherein bureaucracy has deprived mankind of progress, and, had it not been possible to overcome the bureaucratic dictation and even persecution of those who sought to advance medicine, and human health, we would now be, healthwise, in the same Middle Ages from which Appendix A derives its original citations.

Have we forgotten that there was a time when the best science concluded that the World was flat, the sun revolved around the Earth, and that insanity could be relieved by drilling holes in the skull to let the demons out? Have we also forgotten that Galileo, the great scientist who dared to say that the world was round, was persecuted for his effronteries to the scientific world of his time? And, Galileo lived some three centuries after the first statutory reference in Appendix A.

Unfortunately, various "experts" in every age, rooted in tradition, fight change, and developments in science, with deplorable results for public health.



It is well known that sailors of the British navy became known as "Limeys" because part of their diet after 1795 was lemon juice (then called lime juice), taken to prevent scurvy which had been a long-time dread killer. Not as well known is the story of Dr. James Lind, surgeon of the British fleet, who had performed experiments showing that scurvy could be prevented by a bit of lemon or lime juice added to the diet. In 1753 he published a book "A Treatise of the Scurvy", including recommendation of this item for the diet, promptly rejected by the notable Lords of the British Admiralty, who then considered that anyone showing the malaise which is associated with scurvy was nothing more than a "malingerer" requiring the "therapy" of a good flogging.

Following publication of his treatise, Lind's fellow physicians also attacked him. It was 42 years after Dr. Lind's treatise had been published that the British navy finally adopted the simple "ascorbic" regimen Dr. Lind had recommended. Now we know that the Vitamin C in the limes recommended by Dr. Lind is a vital and essential necessity for the diet of mankind.

The Federation urges that for the best "science" to insist that it knows Laetrile is worthless in every case is vainglorious presumption.

In the long upward struggle of man toward his enlightenment and progress from primitive savagery to the light of reason and understanding, countless multitudes of unfortunates have suffered from the persecution, indignities and tortures of their fellows. These persecutions have encompassed almost every field of human activity. For example, Copernicus, more lucky than Galileo, missed by a hair being burned at the stake because he taught that the Earth

was round, and was merely a satellite of the sun, rather than being the "center of the universe" as was then taught by the "great scientists".

*Joseph Lister*—nearly driven out of the medical profession by the British Medical Association because he said that surgery which was not antiseptic gave rise to infection and caused great mortality among patients. Lister in turn had merely followed the teachings of Louis Pasteur, the discoverer of the germ theory of disease.

*Pasteur*—nearly driven from his Chair at the University of Paris by the doctors and physiologists of France.

*Semmelweis*—and in United States Oliver Wendell Holmes, Sr., who discovered the cause of puerperal fever, resulting in death of women in child birth—the cause being the dirty hands of doctors—was nearly driven from the profession. Semmelweis died driven, disgraced, and hounded to his death. Semmelweis had merely insisted upon washing his hands after he came out of the dissecting room, before delivering a woman of child.

*Dr. Jenner*—developed the theory of practice of vaccination as a preventative, and also persecuted by the medical profession.

*Dr. W. W. Keen*—a student of Lister who came back to practice in Philadelphia, virtually driven out of practice by the medical association.

*Robert Koch*—developer of 606, who did work on tuberculosis—persecuted by the German Medical Association.

*William Harvey*—discoverer of the circulation of blood—persecuted by his colleagues.

Countless thousands of sufferers have died because of the ignorance of "current science" and the rigidity and

refusal to admit progress as to new therapies and medicine.

George Washington, the Father of our Country, when 67 years of age and in retirement in Virginia after his Farewell Address, rode out to inspect his plantation, and suffered a cold. The "current science" of his time was mustered, and he received massive bleeding, leeches, and other "remedies" now recognized as barbaric. George Washington succumbed several days later, not of his cold, but primarily due to the treatments rendered by the "medical experts" of his time. He had been denied a condemned minority treatment, which now would be "mandatory", according to current medical thought.

Indeed, orthodoxy thus indirectly killed the Father of our Country, though a life-saving treatment was then in existence, but vetoed by the "learned" majority of practitioners.

More recently, we have the example of Dr. Alexander Fleming, famous pioneer of penicillin, his discovery remaining on the shelf for twelve years while he was designated a "quack" by orthodox practitioners who merely did not understand what he was doing.

William James, father of American Psychology and himself a physician, aptly described the three stages encountered by any new treatment:

1. Entrenched orthodoxy calls it quackery and non-existent.
2. It is admitted to exist, but is written off as unimportant or useless.
3. Finally, its former foes exultantly claim "We helped discover it!"

## CONCLUSION

In the case at bar, FDA has become an instrument of oppression against Respondent Rutherford and other innocent cancer sufferers who merely seek to cling to life, even to regain lost health through those therapies they desire to choose for their own bodies.

Permitting one group to become a state-endowed monopoly is as dangerous in the healing arts as it is in economics or in political thought—perhaps more so, for here we are dealing with life itself. Unfortunately man can be jealous of the known and reluctant to even consider what is new or different. History has shown that men of medicine and bureaucrats can be as narrow and uncompromising as other men. History has shown that many discoveries that we now consider significant were rejected by the majority and their discoverers hounded<sup>11</sup>:

The concept that an infirm person should have a constitutional right to choose any kind of medical treatment available is not a new or modern invention.

Two centuries ago Dr. Benjamin Rush, renowned physician and surgeon general of the Continental Army of the United States, also a signer of the Declaration of Independence, stated that: "Constitution of this republic should make special provisions for medical freedom as well as religious freedom. . . . To restrict the art of healing to one class of men and deny equal privilege to another will constitute the Bastille of medical science. All such laws are

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<sup>11</sup> All of these circumstances are "overlooked" in Petitioner's "Appendix A".

un-American and despotic. They are fragments of monarchy and have no place in a republic."

As it today hounds Glen Rutherford, and others who desire Laetrile, FDA would yesterday have hounded a Lister, a Pasteur, a Jenner, a Koch, an Oliver Wendell Holmes, Sr., or Sir Alexander Fleming. And the day before it would have accused and prosecuted those who dared refuse to bleed during illness or use leeches. From this, progress does not come. From this, man in control may be more comfortable and secure in his comparative ignorance, but he does not learn.

In this context the instant case is of great significance to all Americans. Because of this significance, it is respectfully urged that this Court shall uphold the action of the Court below.

Respectfully submitted,

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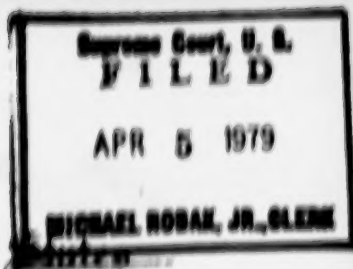
*Exhibit A*



IN THE  
**Supreme Court of the United States**

October Term, 1978

No. 78-605



THE UNITED STATES OF AMERICA, et al.,  
*Petitioners,*

*v.*

GLEN L. RUTHERFORD, et al.,  
*Respondents.*

---

**BRIEF OF AMICUS CURIAE  
THE COMMITTEE FOR FREEDOM OF CHOICE IN CANCER THERAPY  
IN SUPPORT OF RESPONDENTS**

---

**BRIEF OF RESPONDENT IN OPPOSITION**

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IN THE SUPREME COURT OF THE  
UNITED STATES

October Term 1978

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No. 78-605

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THE UNITED STATES OF AMERICA, ET AL.,  
*Petitioners,*

*v.*

GLEN L. RUTHERFORD, ET AL.,  
*Respondents.*

---

BRIEF OF AMICUS CURIAE  
THE COMMITTEE FOR FREEDOM OF CHOICE  
IN CANCER THERAPY  
IN SUPPORT OF RESPONDENTS

---

INTEREST OF AMICUS CURIAE

The Committee for Freedom of Choice in Cancer Therapy is a California Non-Profit Corporation, with State Chapters in each of the Fifty States.

The Committee for Freedom of Choice in Cancer Therapy was formed and operates to, among other things, encourage, foster and conduct programs for the continuing education and training physicians, nurses, technicians, and others as to all matters concerned with the detection, diagnosis, treatment and prevention of cancer, with particular emphasis on metabolic therapy;



to encourage, foster and conduct programs for the continuing education of the public concerning cancer; to further the proper use of metabolic therapy for the treatment and prevention of cancer; to encourage the provision of adequate facilities wherein metabolic cure and treatment may be accorded to cancer patients; and to otherwise encourage, foster and assist the establishment of programs of service to cancer patients.

The Committee for Freedom of Choice in Cancer Therapy receives contributions, legacies and bequests, and proceeds from fund raising events. The Committee for Freedom of Choice in Cancer Therapy uses these receipts for public education, professional education and cancer research. The Committee for Freedom of Choice in Cancer Therapy is actively concerned with the sponsorship of programs which will encourage research into the causes, treatment, cure and control of cancer; programs of public and professional education; and providing information and assistance to cancer victims.

The Committee for Freedom of Choice in Cancer Therapy has consistently gathered evidence and information demonstrating the efficacy of Laetrile when used in conjunction with a total metabolic program. The activities of the Committee for Freedom of Choice have resulted in a widespread recognition of Laetrile, when included as a component and metabolic therapy, as an effective modality in the treatment alleviation and cure of cancer.

The failure of conventional medical therapies to reduce mortality rate resulting from cancer by use of recommended drugs, radiation, and surgery during the past 45 years demonstrates the need for continuing research for a solution to the problem; and specifically, for the need for further liberalization of laws which restrict such research.

## ARGUMENT

1. Whether the safety and effectiveness requirements of the Federal Food, Drug and Cosmetic Act, as applied by the Federal Food and Drug Administration, accomplishes their intended purpose.
2. Whether the constitutional right of privacy protects access to a drug such as laetrile.

### I

#### THE SAFETY AND EFFECTIVENESS REQUIREMENTS OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT AS APPLIED BY THE FEDERAL FOOD AND DRUG ADMINISTRATION FAIL TO ACCOMPLISH THEIR INTENDED PURPOSE.

The Federal Food, Drug and Cosmetic Act, and amendments thereto, were enacted pursuant to the Government's police power to regulate the drug industry because it was felt that the public was largely beyond self-protection from drugs that might be hazardous or ineffective. *United States v. Dotterweich* (1913), 320 U.S. 277, 280; *Weinberger v. Hynson, Westcott and Dunning, Inc.* (1973), 412 U.S. 609, 617-618.

To justify the use of the police power on behalf of the public it must appear, first, that the interests of the public require such regulation and, second, that the means used are reasonably necessary to the accomplishment of the purpose. *Goldblatt v. Hempstead* (1962) 369 U.S. 590, 594-595.

1. While it is conceded that there is a genuine public need to protect the public in general from drugs that are hazardous or ineffective, or both, a close examination of the manner of implementation of the Federal Food, Drug and Cosmetics Act by the Federal Food and Drug Administration reveals that the means used are not effectively accomplishing the purpose of the Act in general, and specifically with reference to the disease cancer. As empowered by statute,<sup>1</sup> the Commissioner of the FDA has promulgated regulations<sup>2</sup> governing New Drug Applications. As the years passed, the impact of these regulations grew:

"There was a steady stream of NDA's under that Act supported by voluminous data. Many new drugs claiming 'me-too' status were marketed illegally or were launched with an advisory opinion of the FDA that they were recognized as safe. It is estimated that by 1969 there were five identical or similar drugs for every drug with an effective NDA. Enormous administrative problems were created. Each NDA contained about 30 volumes, a stack 10 to 12 feet high; and some contained as many as 400 volumes of data." *Weinberger v. Hynson, Westcott & Dunning, supra*, 412 U.S. at page 621.)

The Secretary of Health, Education and Welfare's

<sup>1</sup>21 United States Code, section 371

<sup>2</sup>21 CFR sections 130 et seq.

#### Task Force on Prescription Drugs found:

"The various phases of IND and NDA may require several years, 5 years to complete all the requirements is not considered unusual." (*The Drug Prescribers*, Washington, D.C., U.S. Government Printing Office, 1968, page 119.)

The burdens imposed by the 1962 efficacy requirement have also increased:

"The impact of these requirements on a drug maker was considerable. For example, a Parke-Davis official reported that when the company first marketed a particular epinephrine preparation in 1938, all it had to submit was a 27 page report concerned primarily with safety. In 1948, when it introduced a new expectorant, only a 73 page report was required. Another new drug marketed in 1958 needed a 130 page submission. But in 1962, when Parke-Davis requested FDA approval of its contraceptive Norlestrin, it had to present a report amounting to 12,370 pages. And in 1968, when approval was requested for its new anesthetic Ketamine, the required documents totaled slightly more than 72,000 pages in 167 volumes." (Joseph F. Sadusk, Jr., "The impact of Drug Legislation on Clinical Evaluation of Drugs," paper presented at symposium, Gottlieb Duttweiler Institute, Ruschlikon-Zurich, August 28-29, 1969.)

In October, 1973 Reader's Digest drew the problem to public attention (Walter S. Ross, "The Medicine We Need but Cannot Have," Reader's Digest, October 1973):

"Since 1963, not a single new general-purpose medicine has been introduced in the United States to treat hypertension, even though twenty-three million Americans are affected by the disease. Yet between 1967 and 1971 five such drugs came into general European practice.

"In the same period, ten medications to treat irregular heartbeat came into the market in Europe, yet by mid-1973 only one of these had been approved for U.S. usage.

"At least seven new medications for asthma were introduced in Europe in 1962. By mid-1973 only two could be prescribed in the U.S.A.

"A study conducted by the University of Rochester's Dr. William Wardell found that of the eighty-three new medicines adopted in both Britain and the U.S. between 1962 and 1971, more than half were introduced first in Britain — and an average of 2.8 years elapsed before the FDA allowed them to be sold in this country."

The practical effects of Section 505 (21 U.S.C. section 355) as implemented by the FDA are being felt by the United States citizen:

"Indeed, it is altogether possible that Americans could become a "have not" people in their access to medication with the fruits of chemical and technological improvement created here exported to others but denied us. *Medical Economics* observes that three-quarters of the new drugs being developed by American pharmaceutical firms are going exclusively to people in other lands and are barred from use in America.

"In a similar vein, seven new asthma medications have been introduced in Europe in the past decade, but only two of these have made it to the United States. Forty-seven new medications to treat heart and circulatory problems came on the world market between 1967 and 1971, but only six were made available in this country. Five new drugs for the treatment of hypertension have recently appeared in Europe, but no new general-purpose hypertension medicine emerged in America between 1963 and 1972.

"It is noteworthy that penicillin, if discovered today, probably could not pass the relevant tests of the bureaucracy. After all, the drug does cause unfavorable reactions in some people, and it is less effective in certain cases than in others — considerations that could flunk it on FDA's "safe and effective" meter. Yet penicillin has saved thousands of people from pain and death, and only a fanatic or perhaps a bureaucrat would contend that humanity would be better off

without it."<sup>3</sup>

"Regulatory tightness in the U.S.A. has been such that important pharmaceuticals have been available in other countries and not in America. Importation and use without FDA clearance is not permitted and so the armory of drugs available to the American physician has suffered a relative decline. The contrast in availability has been most marked in cardiovascular, diuretic, respiratory and gastrointestinal areas compared with Britain. In wider and numerical terms "... up to the end of 1971 the overall British lead for mutually available drugs was, in terms of drug-years of prior availability, double that of the United States. In terms of exclusively available drugs, Britain has nearly four times as many as the United States." <sup>4</sup>

The cost of bringing a new drug through the bureaucratic maze to NDA approval has risen from an average of \$1.3 million in 1969 to \$10.5 million in 1970,<sup>5</sup> and to \$24.4 million in 1973.<sup>6</sup>

Since there has been an increasing cost factor in the production of new drugs, the "cost-benefit ratio" becomes exceedingly important to the drug companies. At some point in the NDA process, the drug manufacturer will *patent* the drug so that it may reap the benefits of the research it has incurred and pass these costs on to the consumer and drug company licensees. Since other drug

<sup>3</sup>M. Stanton Evans, "Government Can Be Hazardous to Your Health," *Imprimis*, Vol. 4 No. 6, June 1975

<sup>4</sup>J. E. S. Parker, *Regulating Pharmaceutical Innovation: An Economist's View*, 32 *Food, Drug, Cosmetic L.J.* 160, 172

<sup>5</sup>(H. A. Clymer, "The Changing Costs and Risks of Pharmaceutical Innovation," and V. A. Mund, "The Return on Investment of the Innovative Pharmaceutical Firm," both in *The Economics of Drug Innovation*, ed. J. D. Cooper, Washington, D.C., The American University, 1970).

<sup>6</sup>(National Science Foundation, *A Price Index for the Deflation of Academic R & D Expenditures*, page 2)



companies can use "me-too" copies of an NDA drug (*USI Pharmaceutical Corp. v. Weinberger* (1973), 412 U.S. 655), the patent is of crucial importance in recovering research costs and costs of obtaining the NDA. The concern for profit also makes it clear that it is not profitable to obtain a NDA on a substance, such as laetrile, which is in the common domain as a common chemical and cannot be protected by patent.

An example of this problem is found in *United States v. Evers* (M.D. Ala., 1978), 453 F. Supp 1141. In *Evers, supra*, the drug EDTA (Calcium disodium versenate) was approved by the FDA for chelation treatment of heavy metals poisoning. Dr. Evers was charged with mislabeling of EDTA because he was using it to treat patients for arteriosclerosis, a purpose for which there was no NDA approval. (*U.S. v. Evers, supra*, page 1147.) The District Court observed (at page 1149-1150):

"... New uses for drugs are often discovered, reported in medical journals and at medical meetings, and subsequently may be widely used by the medical profession. But the Federal Drug Administration does not permit the package insert to be amended to include such uses unless the manufacturer submits convincing evidence supporting the change. The manufacturer may not have sufficient commercial interests or financial wherewithal to warrant following the necessary procedures to obtain FDA approval for the additional use of the drug. . . ." (Emphasis added.)

The court in *Evers, supra*, was caught between the Scylla of recognizing that neither a private citizen, the patient nor the physician could afford to undertake the NDA process, and the Charybdis of recognizing the need to protect the public from unsafe and/or inefficient

drugs. Indeed, *Rutherford v. American Medical Association* (CA 7, 1967), 379 F. 2d 641, 643, cert. denied 389 U.S. 1043, the Court of Appeals held that the plaintiffs cancer victims were held to be required to make "an attempted good faith application for application for approval or exemption" for an NDA before their claim could be heard. The Court of Appeals observed (379 F. 2d at page 643):

"... The fact that compliance might be expensive and burdensome is not unfairness in the procedure, but a consequence of a reasonable Congressional scheme for the introduction of new drugs."

While there is "rational justification" for the Federal Food, Drug and Cosmetic Act, amici suggests that compliance has become so expensive and burdensome that there are now "Lines drawn on the basis of wealth . . . (which) . . . are traditionally disfavored" (*Harper v. Virginia Board of Elections* (1966), 383 U.S. 663, 668;), which violates the Equal Protection Clause by discriminating against the average citizen in favor of multi-million dollar drug manufacturers. Cf. *Ortwein v. Schwab* (1973), 410 U.S. 656, 659; *United States v. Kras* (1973), 409 U.S. 434; *Boddie v. Connecticut* (1971), 401 U.S. 371.

The Doctrine of Informed Consent places upon the physician a legal duty to disclose the risks inherent in each of the therapeutic alternatives available to the patient, in order that the patient may make an informed exercise of his choice of a particular course of medical treatment. *Canterbury v. Spence* (CA DC, 1972), 464 F2d 772, 780-782. The Doctrine of Informed Consent in es-

sence gives the patient the right to choose to be a "human guinea pig." It has been suggested that a system of "monitored release" would be a practical solution to the problem, and unproven drugs which pass the test of safety could be granted "conditional acceptance" for use by physicians under a closely monitored system using informed, consenting patients until a sufficient amount of data had been accumulated to establish the drug as effective or ineffective.<sup>7</sup> It would be relatively simple for the FDA to establish protocols for the physician's use in treating the patient and criteria for evaluating the results in terms of efficacy. Such a procedure would reduce the expense of the NDA, would reduce the length of time necessary to complete the NDA procedure, and would give the patient dissatisfied with orthodox treatment an alternative solution to the present dilemma of "orthodox treatment or no treatment."

2. Inherent in the Federal Food, Drug and Cosmetic Act is the premise that, through the statutory scheme enacted, safe and effective drugs will be found for each and every illness. While medicine has made almost miraculous strides in curing many other diseases, such is not the case with cancer. The *6th National Cancer Conference Proceedings*<sup>8</sup> jointly sponsored by the American Cancer Society and the National Cancer Institute (HEW) illustrate the deficiencies of conventional treatment:

At Page 513: *Robert D. Sullivan, M.D.*, Department of Cancer

<sup>7</sup>*People v. Privitera: The Right to Prescribe and Use Laetrile* (1978), 5 Western State University Law Review, 201, 227-229.

<sup>8</sup>Lippincott, 1970

Research, Lahey Clinic Foundation, Boston:

"There has been an enormous undertaking of cancer research to develop anticancer drugs for use in the management of neoplastic diseases in man. However, progress has been slow, and no chemical agents capable of inducing a general curative effect on disseminated forms of cancer have yet been developed."

At Page 33: *William Powers, M.D.*, director, Division of Radiation Therapy, Washington University School of Medicine, St. Louis:

"Although preoperative and postoperative radiation therapy have been used extensively and for decades, it is still not possible to prove an unequivocal clinical benefit from this combined treatment . . . Even if the rate of cure does improve with a combination of radiation and therapy, it is necessary to establish the cost in increased morbidity which may occur in patients with or without favorable response to the additional therapy."

At Page 609: *James F. Holland, M.D.*, Rosewell Park Memorial Institute, New York State Department of Health, Buffalo, N.Y.:

"Human cancer are refractory in large part to cure by the chemotherapeutic approaches which have been tried . . ."

At Page 855: *Philip Rubin, M.D.*, Chief, Division of Radiotherapy, University of Rochester Medical School, Strong Memorial Hospital, Rochester, N.Y.:

"With thousands of lung cancer patients treated by irradiation, the value of radiation therapy should be clearly established or disestablished. The indictment of Radiotherapy in the treatment of this disease by Kraut ('The Question of Irradiation Therapy in Lung Cancer,') JAMA 195 (1966: 177-81) is a carefully researched document that has to be considered. The clinical evidence and statistical data in numerous reviews are cited to illustrate that no increase in survival has been achieved by the addition of irradiation."

At Page 163: *Vera Peters, M.D.*, Princess Margaret Hospital, Toronto, Ont."

"Shimkin (*End Results in Cancer of the Breast*, Cancer 20 (1967): 1039-43) has shown recently that in carcinoma of the breast, the mortality rate still parallels the incidence rate, thus proving that there has been no true improvement in the successful treatment of the disease over the past thirty years, even though there has been technical improvement in both surgery and radiotherapy during that time."

At Page 153: *Robert L. Egan, M.D.*, Professor of Radiology and Chief, Mammography Section, Emory University School of Medicine, Atlanta, Ga.; and *R. Waldo Powell, M.D.*, Associate Professor of Surgery, Department of Surgery:

"The thirty-year monotonous plateau of the death rate for breast cancer has persisted despite physicians' awareness of breast cancer, refinement of methods of inspecting and palpating the breast, educating women in self-examination, improvements in radiotherapy that include supervoltage, use of more extensive surgical procedures, and the use of chemotherapy and hormones."

At Page 421: *I.H. Gillespie, M.D.*; *H. T. Debas, M.D.* and *F. Kennedy*, University Department of Surgery, Western Infirmary, Glasgow, Scotland:

"Since there is yet no sign that either radiotherapy or chemotherapy can offer real therapeutic benefit to patients with gastric cancer, the main hope at present for either cure, or useful palliation, rests with surgical treatment. The many varied surgical approaches do not seem to have made a great difference to the overall outcome in large series of patients, and it seems unlikely that much improvement can be expected from further developments of surgical technique."

At Page 83: *Saul A. Rosenberg, M.D.*, associate professor of Medicine and Radiology, Stanford University School of Medicine, Palo Alto, California:

"Thus, worthwhile palliation is achieved in many

patients however, there still will be the inevitable relapse of the malignant lymphoma, and, either because of drug resistance or drug intolerance, the disease will recur, requiring modifications of the chemotherapy program and eventually failure to control the disease process. With very few exceptions, cure is not achieved despite the dramatic initial benefit which is seen in so many patients."

At Page 379: *John D. Trelford, M.D.*, F.R.C.S., Department of Obstetrics and Gynecology, Ohio State University Hospital:

"At the present time chemotherapy of gynecological tumors does not appear to have increased life expectancy except in sporadic cases . . . There appears to be no satisfactory method of determining to which drug a tumor will be sensitive. The only basis of selecting a drug is by past experience. The problem of blind chemotherapy means not only a loss of the effect of the drugs, but also a lowering of the patient's resistance to the cancer cells owing to the toxicity of these agents . . . At the present time there is no satisfactory method of stimulating or mobilizing the host's immunological defenses to aid in controlling or eradicating the patient's malignancy."

Dr. Hardin Jones of the University of California at Berkeley indicated that, with the exception of child leukemia and possibly Hodgkin's disease, there has been no reduction in the incidence of deaths from cancer in the United States and the western world since 1911, despite the best efforts of medical science; and that cancer victims receiving no medical treatment live longer than victims receiving treatment ". . . and for some of the common kinds of cancers, such as breast cancer, this amounts to a considerable factor, approximately a factor of four (time longer)." (R 507, pp. 4634-4635, 4656-4659)

Counsel for Petitioner acknowledges the severity of



the problem (Petitioner's Opening Brief, fn. 21) by pointing out that the FDA has over 300 oncologic drugs under clinical investigation, and that the NCI screens from 15,000 to 30,000 potential anti-cancer drugs each year.

The ineffectiveness of contemporary cancer treatments coupled with the intensive research to find a cure and the invidious resistance of cancer to cure, strongly emphasizes that at present the standard of "efficacy" applied to cancer by the FDA must be extremely low. This in turn casts doubt upon the existence of a "rational basis" of the "efficacy requirement" as it applies to cancer drugs in general, and laetrile in particular. (*Weinberger v. Hynson, Westcott & Dunning, Inc., supra*) That *United States v. Rutherford*, the present case before this court, was certified as a class action by the trial judge (WD Okla. 1977; 429 FSupp 506) gives strong indication that a great number of people are seeking metabolic treatment which includes administration of laetrile because *there are no* "effective" cancer drugs or treatments, and because they feel that metabolic therapy which includes laetrile is a safer and more preferable alternative to chemotherapy, radiation and surgical treatment.<sup>9</sup> Likewise, the enormous magnitude of the problem created by the FDA's implementation of the NDA policy to laetrile and other non-profitable cancer drugs, and the cancer victim's rejection of orthodoxy's failures, is indicated by

<sup>9</sup>The United States Department of Health, Education and Welfare's National Institute for Occupational Safety and Health has published the *Registry of Toxic Effects of Chemical Substances* (1976), which was written with the objective "to identify all known toxic substances." Laetrile (amyg-

the large quantities of laetrile brought into this country

daline) is not listed therein, apparently because it is not considered toxic; however, toxicity figures are readily available. (Manner, H. W.; *The non-toxicity of Amygdalin to laboratory mice*, Sci. Biol. J., p. 347-349 (May-June 1977).) A comparison of Laetrile toxicity with the toxicity of other common drugs in terms of milligrams per kilogram of body weight:

Test Animal	Laetrile (Amygdalin)	Amphetamine	Aspirin	Digitalis
Mouse, oral	150 mg/kg	15 mg/kg	815 mg/kg	3.5 mg/kg
Mouse, intraperitoneal	9500 mg/kg	23 mg/kg	195 mg/kg	5.5 mg/kg
Mouse, intravenously	9100 mg/kg	18 mg/kg	681 mg/kg	20 mg/kg
	Tetracycline	Cytosan*	Actino-mycin D	Vitamin B <sub>1</sub> (Thiamine)
	808 mg/kg	91 mg/kg	13 mg/kg	8221 mg/kg
	125 mg/kg	210 mg/kg	.07 mg/kg	220 mg/kg
	291 mg/kg	160 mg/kg	.016 mg/kg	89 mg/kg

It is clear that the lower the figure for the lethal dose, the more toxic the drug is. Conversion to 'Probable Human Lethal Dose' classification applicable to the foregoing drugs is as follows (Casarett, L. J. and J. Doull, *Toxicology*, Macmillan Pub. Co. (1975).):

Toxicity	Commonly Used Term	Probable Human Lethal Dose 70 kg. (150 lb.) man
6	Supertoxic	less than 5 mg/kg — less than 7 drops
5	Extremely toxic	5 to 50 mg/kg — 7 drops to 1 tsp
4	Very toxic	50 to 500 mg/kg — 1 tsp to 1 ounce
3	Moderately toxic	500 mg/kg to 5 g/kg — 1 oz to 1 pint
2	Slightly toxic	5 to 15 grams/kg — 1 pint to 1 quart
1	Practically nontoxic	over 15 grams/kg — over 1 quart

As these authorities show, Laetrile is only slightly toxic in injectable form and is safer than all other injectables compared to it; and in oral form is safer than amphetamines, and almost as safe as aspirin.

Counsel for Petitioner United States correctly acknowledges that "No drug is completely "safe" in the lay person's sense of the word, since every drug — aspirin not excepted — involves risks." (Petitioner's Brief, p. 21.)

illegally<sup>10</sup>, the number of governmental civil actions to prevent manufacture and distribution,<sup>11</sup> legal actions brought by cancer victims,<sup>12</sup> the large number of cancer victims making the "Mexican laetrile connection,"<sup>13</sup> and the number of cancer victims within the United States being treated with laetrile.<sup>14</sup>

The issue of the toxicity of laetrile is a phantom issue, in any event, as University of New Mexico School of Law

<sup>10</sup>*United States v. Richardson* (CA 9, 1978) 588 F. 2d 1235, *United States v. Luther* (CA 9, 1975), 521 F. 2d 408; *United States v. Westover* (CA 9, 1975), 511 F. 2d 1154; *United States v. Medina-Carbajal*, Cr. No. 15896 (S.D. CA, 1973); *United States v. De Garrido*, Cr. No. 16053 (S.D. CA, 1973) *United States v. Guillent*, Cr. No. 74-405 (S.D. CA, 1974); *United States v. Bonilla* Cr. No. 75-0732 (S.D. CA, 1975); *United States v. Alvarez-Horta*, Cr. No. 75-1026 (S.D. CA, 1975); *United States v. Weisman*, Cr. No. 75-1493 (S.D. CA, 1975); *United States v. Gonzales-Pacheco*, Cr. No. 75-1921 (S.D. CA, 1975); *United States v. Mejia-Mejia*, Cr. No. 76-0050 (S.D. CA, 1975); *United States v. Turner* (CA 2, 1977), 558 F. 2d 46.

<sup>11</sup>*United States v. Articles of Food and Drug*, (E.D. WI, 1978), 449 FSupp 497; *United States v. Spectro Foods Corp.*, (CA 3, 1976), 544 F. 2d 1175; *United States v. General Research Laboratories* (C.D. CA, 1975), 397 FSupp 197; *United States v. Article of Drug . . . Laetrile* (Krebs Laboratories (DID, 1965), No. 8507; *United States v. Hawk* (S.D. CA, 1963), Civ. No. 8082; *United States v. Mosinee Research Corp* (CA7, 1978), 583 F. 2d 930; *Hanson v. United States* (D. MN, 1 976), 417 FSupp 30, aff'd 540 F2d 947 (CA8, 1976); *United States v. Earthco* (C.D. CA, 1979), Civ. No. 78-3602; *Gadler v. United States*, (D MN, 1977); 425 FSupp 30.

<sup>12</sup>*Rizzo v. United States* (E.D. NY, 1977), 432 FSupp 356; *Carnohan v. United States* (S.D. CA, 1977), Civ. No. 77-0100; *Mattson v. United States* (N.D. CA, 1977), Civ. No. 77-0300; *Keene v. United States* (S.D. W. Va., 1976), Civ. No. 76-249; *Rutherford v. American Medical Ass'n* (CA 7, 1967), 379 F. 2d 641, cert. denied, 389 U.S. 1043; *Durovic v. Richardson*, (CA 7, 1973), 479 F. 2d 242, cert. denied 414 U.S. 944.

<sup>13</sup>17,000 per year, according to the *Rochester* (Minn.) *Post-Bulletin*, series of January 21-25, 1974.

<sup>14</sup>At least 75,000 cancer victims are currently treating with laetrile. Harper, Harold W., M.D. and Michael L. Culbert *How You Can Beat the Killer Diseases*. Arlington House (1978).

assistant professor Robert L. Schwartz observes:<sup>15</sup>

"... Before laetrile became a political issue, almost all the formal medical research demonstrated, or assumed that laetrile was nontoxic. The only evidence the medical profession has offered to show that it is poisonous appears to be in direct support of the medical profession's political arguments. . . . No study has shown that the dosage recommended by physicians who prescribe laetrile in the United States even approaches the toxic level."

It must also be noted that the very concept and future of metabolic therapy — the use of vitamins, minerals and enzymes to improve the body's over-all health and cancer-fighting capabilities — will be affected by the outcome of this case, since vitamin-mineral-enzyme combinations are not proven "safe and effective" for the treatment of cancer and are therefore mis-branded. *United States v. Evers, supra*. Nobel Prize Laureate Linus Pauling has found evidence that mega-doses of vitamin C are efficacious in treating cancer; Frank Chytell, M.D. and David Ong, M.D. of Vanderbilt University have found evidence that mega-doses of vitamin A are efficacious in treating cancer; and Warren Bollag, M.D. of Hoffman-LaRoche Research Laboratory in Basel, Switzerland has found vitamin A to be efficacious in treating topical cancer tumors, in addition to thousands of other physicians who are currently using vitamins, minerals and enzymes for cancer treatment. Concededly, the use of these innocuous substances for treatment of cancer will cause them to be classified as

<sup>15</sup>65 American Bar Association Journal, 224, 225 (February 1979).

drugs because of the intended use of the substance. 21 U.S.C. section 321(g)(1)(B); *United States v. "Vitasafe Formula M,"* 226 F. Supp 266, 278 (DNJ 1964), remanded on other grounds, 345 F. 2d 864 (CA 3, 1965) cert. denied, 382 U.S. 948. Nor is it likely that those with the financial capability of pursuing the NDA process — the major drug companies — will be willing to do so since vitamins, minerals and enzymes are currently in the common domain and, hence, there are no profits to be made nor even the opportunity to recover costs of the NDA process.<sup>16</sup>

Finally, it must be noted that one of the risks involved in the "New Prohibition" imposed against laetrile is that cancer victims who reject orthodox treatment are forced into "self-treatment" which, because of the patient's ignorance of medical matters, can be very hazardous.<sup>17</sup>

Counsel for amicus suggests that, notwithstanding the Court's ruling on the right of privacy issue, this Court should find that the means used by the FDA in its quest for "safety and efficacy" are not reasonably related to the intended objectives.

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<sup>16</sup>It is also clear that the NDA process must be followed for combinations of drugs, i.e., the combination must be generally recognized as safe. *United States v. Article of Drug Entrol-C Medicated* (CA 9, 1975), 513 F. 2d 1127.

<sup>17</sup>As pointed out by amici State of California and American Cancer Society briefs in the case of Jo Anne Pye, who may have died of cyanide toxicity and who was treating herself. The autopsy report also reflected fluid in the lungs, and kidney and liver failure. Statements from witnesses reflect that Jo Anne Pye was self administering laetrile rectally. Rectal administration of laetrile is strongly discouraged by physicians because of the high danger involved. See Appendix A17

## II

### THE CONSTITUTIONAL RIGHT OF PRIVACY PROTECTS ACCESS TO A DRUG SUCH AS LAETRILE.

It is conceded at the outset that the constitutional guarantee of personal privacy (*Palko v. Connecticut* (1937), 302 U.S. 319) is not absolute, and that it is to be balanced against important state interests in regulation (*Roe v. Wade* (1973), 410 U.S. 113, 154). However, *Roe v. Wade* also notes (410 U.S. at 155):

"Where certain 'fundamental rights' are involved, the Court has held that regulation limiting these rights may be justified only by a 'compelling state interest,' (citations) and that legislative enactments must be narrowly drawn to express only the legitimate state interests at stake. (citations)"

Since it is well established that the purpose of the Federal Food, Drug and Cosmetic Act is to protect the public at large from unsafe and ineffective drugs, the right to privacy must be weighed against this state interest.

An examination of recent state and federal right to privacy cases reveals that there is an *additional* factor which the courts consider — whether the impact of the exercise of the right will affect *only* the individual concerned, or whether it will affect the *public at large*. *Roe v. Wade, supra* (approving abortions for the class 'pregnant women desiring,' while affirming the state's right to regulate matters pertaining to the health of members of that class); *Doe v. Bolton* (1973), 410 U.S. 179 (striking state regulations pertaining to abortions for the class 'pregnant women' not rationally related to safety,



while affirming the physician's "independent judgment"); *Griswold v. Connecticut* (1965), 281 U.S. 479 (affirming contraception for the class 'women' under right to privacy, while affirming the state's right to ban unsafe contraceptives); *Eisenstadt v. Baird* (1972), 405 U.S. 438 (no rational basis to outlaw contraceptives for the class 'single women' but not the class 'married women'; violated right of privacy); *Loving v. Virginia* (1967) 388 U.S. 1 (no rational basis for invading right of privacy of 'married people' to prevent interracial marriages); *Whalen v. Roe* (1977), 429 U.S. 589 (right to privacy bowed to state registration of 'Schedule II' drug users because the class of drugs was subject to abuse by the class of 'drug users'); *Planned Parenthood of Missouri v. Danforth* (1976), 428 U.S. 52 (no rational basis to prohibit saline amniocentesis abortion procedure to class, because safe, as against right to privacy); *Carey v. Population Services International* (1977), 431 U.S. 678 (no rational basis to prohibit certain contraceptive devices proven safe to class of 'users' in face of right to privacy); *Fitzgerald v. Porter Memorial Hospital* (CA 7, 1975), 523 F. 2d 716 (Right to privacy bows to health safety precautions in maternity delivery room); *Jacobson v. Massachusetts* (1905), 197 U.S. 1 (right to privacy bows to compulsory smallpox vaccination to protect public at large from health hazard of possible epidemic); *Gray v. State* (Alaska, 1974), 525 P. 2d 524 (right to privacy shields ingestion of food, beverages, other substances, absent a compelling state interest); *People v. Raven* (Alaska, 1975), 537 P. 2d 491 (right to privacy protects possession, ingestion of marijuana to class of users

because no legitimate state interest; right to privacy bows when adolescents or driving under the influence involved because legitimate state interest); *White v. Davis* (Cal., 1975), 13 C. 3d 757 (Right to privacy protects college classroom, class 'students,' from governmental spying); *Burrows v. Superior Court* (Cal., 1974), 13 C. 3d 238 (Right to privacy protects bank records unless probable cause and warrant); *Valley Bank of Nevada v. Superior Court* (Cal., 1975), 15 C. 3d 652 (civil discovery shall be weighed against right to privacy prior to disclosure of bank records); *Britt v. Superior Court* (Cal., 1978), 20 C. 3d 844 (Right to privacy protects medical records against civil discovery unless shown relevant to the case); *Tavernetti v. Superior Court* (Cal., 1978), 22 C. 3d 187 (Right of privacy protects against citizen eavesdropping on telephone); *Matter of Quinlan* (N.J., 1976), 70 N.D. 10, 355 A. 2d 647 (state interest in preservation of life bows to right of privacy in choice to refuse life-preserving medical treatment); *Estate of Brooks* (Ill., 1965) 32 Ill. 2d 361, 205 N.E. 2d 435 (same); *Superintendent of Belchertown State School v. Saikewicz* (Mass., 1977), 379 N.E. 2d 418 (right to privacy embraces cancer patient's right to refuse chemotherapy to treat Leukemia; state has no interest in intervening in choice of treatment). The Massachusetts Supreme Court observed in *superintendent of Belchertown, supra*, (379 N.E. 2d at 426):

"The constitutional right to privacy, as we conceive it, is an expression of the sanctity of individual free choice and self-determination as fundamental constituents of life. The value of life as so perceived is lessened not by a decision to refuse treatment, but by

*the failure to allow a competent human being the right of choice."* (Emphasis added.)

*The individual right to choose one's own medical treatment, or to refuse medical treatment altogether, is a choice which does not affect the public at large.* While there is a rational basis for the government to wish to protect the public at large from unsafe, ineffective drugs, this 'compelling state interest' diminishes considerably and the right to privacy is correspondingly strengthened in two situations: (1) where the patient makes a personal choice to select one cancer treatment in preference to another, or declines treatment; and (2) where the patient chooses to become a 'human guinea pig' after being fully advised of the risks inherent in each of the accepted therapeutic alternatives, and of the experimental treatment.<sup>18</sup> The seriousness of the impact of cancer on society and the individual,<sup>19</sup> and the shortcomings of present treatments readily explains the "political revolt against what many people find to be unwarranted

<sup>18</sup>Over 300 oncological drugs are under clinical investigation, and 97,800 individual cancer victims were 'human guinea pigs' in 1977. Brief for the United States, fn. 21. Presumably, these drugs had shown promise and had been determined to be 'safe' at certain dosages, and are being tested on humans to establish whether or not they are effective.

<sup>19</sup>"1977 *Cancer Facts and Figures* by the American Cancer Society estimates that 1977 will have produced an estimated 690,000 new cancer cases; and that over 54 million Americans now living will eventually have cancer, which is one out of every four Americans living. The pamphlet also states that over the years cancer will strike in approximately two of every three families, that in the 1970's there will be an estimated 3.5 million cancer deaths, 6.5 million new cancer cases, and more than 10 million people under medical care for cancer. Only about 1/3 of all people who get cancer this year will be alive five years after treatment, according to the publication." *Rutherford v. United States* (WD OK, 1975), 438 FSupp 1287, fn. 27.

government intervention in their private lives."<sup>20</sup>

There is a relatively small class within the much larger class 'cancer patients' who wish to include laetrile in their treatment. They are willing to be the informed, consenting 'guinea pigs' necessary to prove or disprove the efficacy of laetrile. They are geographically distributed throughout the United States, and are not able to participate in a centrally located program such as the National Cancer Institute might offer, yet they do wish for medical care and supervision while pursuing their chosen course of unorthodox therapy, as a preference to self-treatment. Many have returned from the laetrile clinics in Mexico, only to find that physicians are reluctant to take them as patients because of the illegality associated with laetrile and the risk to their medical licenses. Some of these cancer victims have been 'written off' by orthodoxy, and all wish to improve the quality of their lives. The wide anti-laetrile publicity generated by the American Cancer Society, the American Medical Association, the Federal Food and Drug Administration, and other political opponents of laetrile, has put them on notice that most medical authorities regard laetrile as worthless, a sham, a fraud, so that they are aware of the risks undertaken by becoming a 'human guinea pig.' *The risk of knowingly choosing to become a 'human guinea pig' does not affect the public at large; it affects only the individual making the choice to take the risk.* Just as the right to privacy protects the individual's right to refuse treatment (*Superintendent of Belchertown,*

<sup>20</sup>Schwartz, *Laetrile: The Battle Moves into the Courtroom*, 65 American Bar Association Journal, 224, 226 (February, 1979)

*supra*; *Matter of Quinlan, supra*), the right of privacy should protect the individual's right to intelligently choose an unorthodox medical treatment, notwithstanding the recent California Supreme Court decision in *People v. Privitera* (Cal., 3-15-79), \_\_\_ C. 3d \_\_\_,<sup>21</sup> to the contrary.

The error that the California Supreme Court has made in *People v. Privitera, supra*, is to interpret *Whalen v. Roe, supra* to mean that (1) the state may totally prohibit all drugs within a certain class; and (2) that the right to privacy does not include medical treatment. The California Supreme Court stated (slip opinion, p. 5):

"However, a fundamental privacy right is not at stake here. The interest defendants allege is, apparently, the interest in independence in making certain kinds of

<sup>21</sup>In an incredibly shallow opinion, the California Supreme Court upheld a conviction obtained under the "anti-cancer quackery" statute enacted by the California legislature in 1959. The legislative findings (California Health & Safety Code section 1700) indicate an intent to protect against "misrepresentations . . . misleading to the public" because "It has established that the accurate and early diagnosis of many forms of cancer, followed by prompt application of methods of treatment which are scientifically proven, either materially reduces the likelihood of death from cancer or may (sic) materially prolong the useful life of individuals suffering therefrom."

Following the "rational basis test," the California Supreme Court found "a fundamental privacy right is not at stake here," that the 'important decisions' recognized by the United States Supreme Court ". . . do not include medical treatment," and that a rational basis existed for the statute. Dissenting Justice Newman detected no compelling need to abridge the right to privacy; and dissenting Justice Bird adopted in full the extremely lucid, well written opinion of Justice Staniforth in the lower court.

Thus has California abandoned the mainstream of opinion set by other state supreme courts (*Matter of Quinlan, supra*; *Superintendent of Belchertown, supra*; *Gray v. State, supra*), leaving matters in the hands of the legislature, where a bill is being introduced to legalize laetrile, as has now been done in 19 other states.

important decisions.' (*Whalen v. Roe* (1977) 429 U.S. 589, 599-600.) But the kinds of 'important decisions' recognized by the high court to date as falling within the right to privacy involve 'matters relating to marriage, procreation, contraception, family relationships, and child rearing and education.' (*Whalen v. Roe, supra*, 429 U.S. at p. 600, fn. 26 quoting *Paul v. Davis* (1976) 421 U.S. 693, 713), but do not include medical treatment.

"For this reason defendants' reliance on *Roe v. Wade, supra*, 410 U.S. 113, is misplaced. . . ."

*Whalen v. Roe, supra*, dealt with the state's right to require registration and regulation of dangerous drug prescriptions (opium and derivatives, cocaine, methadone, amphetamines and methaqualone), while recognizing that a state could *not* ban all drugs within a class that had medical usage, and that there was, indeed, a right to privacy included in medical treatment. The Court observed (429 U.S. 603):

". . . Clearly, therefore, the statute did not deprive the public of access to these drugs.

"Nor can it be said that any individual has been deprived of the right to decide independently, with the advice of his physician, to acquire and to use needed medication. Although the State no doubt could prohibit entirely the use of *particular* Schedule II drugs, it has not done so. This case is therefore unlike those in which the Court held that a total prohibition of certain conduct was an impermissible deprivation of liberty. Nor does the State require access to these drugs to be conditioned on the consent of any State official or other third party. Within dosage limits which appellees do not challenge, the decision to prescribe, or to use, is left entirely to the physician and patient."

What the California Supreme Court has done is upheld a ban on *all* experimental drugs unless *proven*



safe and effective,<sup>22</sup> thus limiting California cancer victims to the choice of "orthodox treatment" or declining treatment altogether, denying them access to experimental programs, whether government sponsored or otherwise. Such law clearly violates the spirit and letter of *Whalen v. Roe*, *supra*, *Roe v. Wade*, *supra*, and other cases affirming the right to privacy relating to medical care.

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<sup>22</sup>California Health & Safety Code section 1707.1 provides:

"The sale, offering for sale, holding for sale, delivering, giving away, prescribing or administering of any drug, medicine, compound or device to be used in the diagnosis, treatment, alleviation or cure of cancer is unlawful and prohibited unless (1) an application with respect thereto has been approved under Section 505 of the Federal Food, Drug and Cosmetic Act (21 USC Section 355), or (2) there has been approved an application filed with the board setting forth:

(a) Full reports of investigations which have been made to show whether or not such drug, medicine, compound or device is safe for such use, and whether such drug, medicine, compound or device is effective in such use;

(b) A full list of the articles used as components of such drug, medicine, compound or device;

(c) A full statement of the composition of such drug, medicine, compound or device;

(d) A full description of the methods used in, and the facilities and controls used for, the manufacture, processing and packing of such drug, medicine, or compound or in the case of a device, a full statement of its composition, properties and construction and the principle or principles of its operation;

(e) Such samples of such drug, medicine, compound or device and of the articles used as components of the drug, medicine, compound or device as the board may require;

(f) Specimens of the labeling and advertising proposed to be used for such drug, medication, compound or device."

## CONCLUSION

It is respectfully submitted that the judgment of the court of appeals should be affirmed on the grounds relied on by the district court. *United States v. New York Telephone Co.* (1977), 434 U.S. 159, 166 n. 8.

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**APPENDIX**  
**THE FOCAL ACTION OF AMYGDALIN**  
**IN THE METABOLIC THERAPY OF CANCER**

By Robert W. Bradford and Henry W. Allen

In any discussion of amygdalin and its metabolism it becomes necessary as a first step to distinguish between the terms "amygdalin" and "laetrile." Fortunately, a great effort has recently been made to clarify these words.

Drug containers presently used in cancer therapy which bear the label "Laetrile" contain no laetrile but only amygdalin. Laetrile, as properly — if not commonly — defined, is not at present commercially available.

Amygdalin is a specific natural substance which may be isolated from various sources, notably apricot and peach kernels, cherry stones, bitter almonds and other seeds of the genus Prunus. Chemically, it is D-1-mandelonitrile gentiobioside, or D-mandelonitrile coupled to the disaccharide, gentiobiose, formed from two molecules of D-glucose.<sup>1</sup> The naturally occurring cyanohydrins of this

type are known as cyanogenic glycosides.<sup>52</sup> The empirical formula for amygdalin is  $C_{20}H_{27}NO_{11}$ .

In contrast, laetrile is D-l-mandelonitrile glucuronide formed from the same aglycon but with the disaccharide replaced by glucuronic acid. The term "laetrile" is frequently used by laymen to designate all cyanogenic glycosides. The term "laetrile" is generally used by chemists to designate a specific biosynthesized molecule from the degradation product of amygdalin having the empirical formula  $C_{14}H_{15}NO_7$ .

#### BIOCHEMICAL PATHWAYS (Introduction)

The biochemical pathway of amygdalin will be briefly described. The first reaction is the cleavage of the exposed glucose at the oxygen linkage to the inner sugar. This is accomplished by the enzyme Beta-glucosidase found in various tissues<sup>53</sup> and bound to the inside of the lysosomal membrane.<sup>54</sup> One molecule of glucose is split off leaving the residue known as prunasin. The action is repeated with the liberation of the second glucose and the formation

of D-d-mandelonitrile.<sup>2</sup> This compound also contains a secondary alcohol group, which leads to some intriguing biochemical considerations concerning the detoxification process in humans of alcohols and amines, which is discussed later.

#### STEREOCHEMISTRY OF AMYGDALIN

The scientific designation for amygdalin, D-l-mandelonitrile beta-diglucoside describes the compound's configuration, optical activity and composition.

The capital "D" designates the absolute configuration in a configurational sense only. The lower case "l" denotes the direction that polarized light rotates when passed through the complete compound in solution under specified conditions, "l" denoting a left or (-) rotation.

"Mandelonitrile," one of the molecules forming the amygdalin compound, is composed of benzaldehyde and cyanide. The mandelonitrile as a separate compound is dextrorotatory or d-Mandelonitrile.<sup>83</sup>



The "Beta" denotes one of two possible links between mandelonitrile and the diglucoside, the other being designated "Alpha."

The "diglucoside" is a compound molecule making up amygdalin. The diglucoside in this molecule consists of two d-glucose units having a beta linkage, known as gentiobiose.

The optical rotation of the d-gentiobiose portion as a separate compound undergoes mutarotation in aqueous solution but is stable within the amygdalin compound.<sup>86</sup>

The optical activity of a compound which is either dextrorotatory (d), rotating a light beam to the right, or levorotatory (l), bending the light beam to the left, is determined by optically active carbon centers in the compound. Carbons having four single bonds, with each bond holding a different atomic structure, become optically active centers. In the case of amygdalin, there are 11 active centers, five in each sugar and one at the junction connecting the phenyl group to the "CN" group in the

mandelonitrile portion or, one in the mandelonitrile grouping in the molecule.

The active centers in the gentiobiose are stable under normal environmental and manufacturing processes typical of sugars. However, the asymmetric optically active center at the CN group will undergo racemic modification (with reference to this single carbon) under conditions such as described below and an epimeric modification of the amygdalin compound results.<sup>80</sup>

The specific sense of optical rotation caused by an asymmetric carbon center depends on the orientation of the groups held by the carbon. In space there are only two possible configurations which result in the dextro or levo optical rotation. If all the active centers change from one state, to another, the compounds are mirror images and are referred to as enantiomers.

These enantiomers will then be either dextro or levorotary and an equal mixture of the enantiomers is called a racemate, where 50% of the enantiomers are dextrorotary and 50% are levorotary, the compound then, is said to be,

optically inactive and an example would be dl-lactic acid or  $\pm$  lactic acid.

In the case of amygdalin, only the asymmetric carbon at the CN group shifts isomerically so that enantiomers of amygdalin do not occur. This type of modification is referred to as eperimerization (some, but not all, active centers shift), so that the term "racemic amygdalin" or racemized amygdalin is not appropriate. The term eperimeric amygdalin would be correct.

When epimerization occurs in solution with amygdalin, the normally occurring isomer, usually  $-37^{\circ}$ , rotates to a nominal  $-59^{\circ}$  at which point an equilibrium state is reached. Therefore, the common term "dextro amygdalin" is not appropriate inasmuch as all eperimeric configurations are levorotary. The indicated optical activity can be modified by the hydrolysis of mandelonitrile by the action of alkali to mandelic acid.<sup>79</sup> However, this is no longer amygdalin and does not occur with the extraction procedures which have been in common use.

The optical activity of the three components comprising amygdalin (two glucose residues and mandelonitrile) are all dextrorotatory, however, when the individual units, d-mandelonitrile along with two d-glucose residues are combined to form the intact molecule, amygdalin, the optical activity is levorotatory. The physical mechanism involved in the molecular interactions is obscure and is not theoretically predictable by noted authorities in the field so that the value of optical activity must be obtained empirically.

#### Mechanism of Reaction

The carbon in the epimeric center is bound to two electron-withdrawing groups, the phenyl group (benzene ring) and the nitrile group (CN), leaving that carbon with a partial positive charge. This phenomena is referred to as the "inductive effect." The result is that the proton also bound to this center, having a positive charge, tends to be repelled or is more loosely bound to the carbon. In a basic medium containing hydroxyl groups ( $\text{OH}^-$ ) the proton ( $\text{H}^+$ ) is pulled off and combines with  $\text{OH}^-$  forming water

( $\text{OH}^- + \text{H}^+$ ). When the proton leaves the asymmetric carbon, a "site" is formed which permits any of the three remaining groups to interchange with it and move into the position vacated by the proton. Whichever group moves, that position vacated by the group becomes a "site" which in turn recovers the proton from the dissociated water to regenerate the hydroxyl ion ( $\text{OH}^-$ ).

The amygdalin molecule is in a state of equilibrium between the two eperimeric forms and is in a constant state of change as long as the molecule is in a basic medium. It requires only a trace amount of base ( $\text{OH}^-$ ) to initiate epimerization<sup>80</sup> and, in the absence of optically active impurities, accounts for the variations reported in the literature for optical activity (Value reported in the 9th Edition of the Merck Index -  $42^\circ$ ).

The epimerization of amygdalin results in different solubilities due to the hydroxy ( $-\text{OH}$ ) group exposure as the various other groups within the molecule shift in relation to each other. The solubility of a given epimeric configuration could therefore either increase or decrease

depending upon the form. In the case of amygdalin the epimerization increases the solubility in water from a nominal .125 mg/ml to .350 mg/ml. Increased solubility in water for injectables can be achieved, however, by appropriate processing in aqueous solution or by lyophilization.

#### ENZYMIC ACTIVITY VERSUS STEREOCHEMISTRY

The enzymic sequential cleavage of the diglucoside from mandelonitrile is independent of epimerization. The receptor site of the enzyme beta-glucosidase, recognizes first the terminal D-glucose and second, the adjacent D-glucose, independent of the asymmetric carbon center orientation in the mandelonitrile grouping. Furthermore, the decomposition of mandelonitrile to benzaldehyde and hydrogen cyanide is alkaline hydrolyzed in vitro, rather than enzymatic, and epimerization would not affect this decomposition.<sup>2,79</sup> Alkaline hydrolyzation is noted when cyanohydrins, including mandelonitrile, are placed in blood



plasma with the resultant detection of cyanide in a very short period of time.<sup>81</sup>

As previously described, amygdalin, even in a solution having a trace amount of base will undergo eperimerization.<sup>80</sup> Amygdalin, injected, therefore will undergo eperimeric modification because the blood is slightly basic and heavily buffered with a normal pH of 7.4.<sup>55</sup> Likewise, oral amygdalin, when it reaches the alkaline medium of the intestines, would also undergo epimeric modification.

Claims alleging that levorotatory amygdalin is the only effective compound and that the dextro material is ineffective are misleading since as previously discussed, there is no such compound as dextro amygdalin, all epermic forms being levorotatory.

Confusion over the effects of stereochemistry of amygdalin arises from the failure to distinguish the mechanisms of plant reactions from those of animal or man, and from standard stereo notations in some early works.<sup>79</sup>

Enzymatic hydrolysis of amygdalin by emulsin in almonds was first reported by Woler and Liebig (1837).

Haisman and Knight (1967) concluded that emulsion contained three enzymes, two Beta-glucosidases which convert amygdalin to prunasin then to mandelonitrile. The third enzyme catalyzes the dissociation of mandelonitrile of mandelonitrile to benzaldehyde and HCN,<sup>83</sup> this enzyme oxynitrilase or hydroxynitrile lyase leads to specificity of mandelonitrile, but this is a plant enzyme and is not available in man.<sup>84,85</sup> The alkaline hydrolysis of mandelonitrile in animal or man eliminates the stereo specific requirement for decomposition.

Furthermore, as previously mentioned, epermerization will occur in blood plasma and the asymmetric carbon at the nitrile group will be in a constant state of change from one isomer to another, so that any epermeric modification produced commercially is therapeutically inconsequential.

It should be pointed out however, that the rotation of amygdalin is a result of manufacturing processes in common use and any alteration of the manufacturing process in common use would introduce an unknown variable

and would be in contrast to the good manufacturing practices code of the Federal Food and Drug Administration.

It should also be noted that earlier works referred to dextro and levo amygdalin, but it has been pointed out that the term dextro or -d- is inappropriate.<sup>79</sup> The notations dextro and levo referred to the mandelic group only rather than to the entire molecule. In present terminology, the prefixes "d" and "l" refer to the behavior of the entire molecule in the polarimeter.

There is nothing in the literature, theory or practice to substantiate that epimerization of amygdalin affects its therapeutic efficacy which is in good agreement with the empirical evidence in the amygdalin factories and clinics over the past years. The amygdalin in common use has been a partially epimerized aqueous solution of approximately three grams in 10 ml of water and derived from non-buffered alcohol extractions. The nominal rotation of this aqueous solution is  $-45^{\circ}(\alpha) \frac{20}{D} = -45^{\circ}$ ,  $c = 0.30$ .

The amygdalin used for pharmaceutical preparations (powder) conforms to the standard identification specification IS-630-RO<sup>82</sup> as submitted to the federal court. The optical rotation of  $-37.6^{\circ}$  to  $-42^{\circ}$  is common with the extraction procedures which have been in common use.

### CYANIDE CLEAVAGE

#### FROM MANDELONITRILE UNDER BASE CONDITIONS

Mandelonitrile consists of a phenyl group (benzene ring) connected to an asymmetric carbon which in turn is connected to a hydroxy group (OH), a nitrile group (CN) and a hydrogen (H).

The hydrogens on both the hydroxy group and the asymmetric carbon are "active," and are able to dissociate under basic conditions, or in a hydroxyl ( $\text{OH}^-$ ) environment.<sup>55,80</sup> The basic cleavage mechanism involves the proton  $\text{H}^+$  in the OH group binding to a solvent hydroxyl group,  $\text{OH}^-$ , leaving an electron on the oxygen.

The oxygen, following the removal of the proton, then forms a double bond with the asymmetric carbon (which

would result in a fifth bond to the carbon), which then results in the release of the nitrile group (CN) as  $CN^-$ .

When the nitrile group leaves the asymmetric carbon, it also takes with it one electron yielding  $CN^-$ , and the electron left in the oxygen when the proton ( $H^+$ ) dissociated fills the vacancy in the asymmetrical carbon yielding a carbon-oxygen double bond.

The liberated  $CN^-$  then interacts with the dissociated water ( $OH^- + H^+$ ) and combines with the proton  $H^+$ , generating HCN or hydrogen cyanide.

The CN cleavage from the asymmetric carbon in the presence of the hydroxyl ion ( $OH^-$ ) occurs with free mandelonitrile, but is stable with either amygdalin or Laetrile, because the proton (H) in the OH group is replaced by a bond to carbon in the adjacent glycon (glucose or glucuronic acid).

### BETA-GLUCOSIDASE

The availability of beta-glucosidase is an important consideration in amygdalin therapy. One of the primary

sources of beta-glucosidase is the gastrointestinal flora. It is well known that the diet influences the balance of these gastrointestinal microorganisms and their beta-glucosidase activity.<sup>65</sup> Beta-glucosidase is produced in large amounts by the microorganisms Enterococci found in the lower section of the small intestine, large intestine and rectum, with its peak concentration in the large intestine.<sup>55</sup> Large amounts of beta-glucuronidase are also produced in the intestinal flora by Escherichia coli.<sup>55</sup>

Studies have shown that populations which have largely vegetarian diets with little fat or animal matter have a lower incidence of colon cancer and higher beta-glucuronidase activity than do populations which ingest large amounts of fat and animal protein.<sup>65</sup>

Beta-glucosidase is found in soluble form in the liver and intestines and does not exhibit latency.<sup>66</sup> Beta-glucosidase is found in insignificant or trace amounts in the blood in the order of .00016 micromoles per liter.<sup>67</sup>

Beta-glucosidase is membrane-bound in lysosomes on the inside of the bilipid membrane and does not "leak" out



of the lysosome. Therefore, it is not typically available in any appreciable concentration in the plasma or matrix of the cancer or hostal cells.<sup>54</sup> For this reason little or no direct hydrolysis is manifested with intratumoral injections of amygdalin.

Fasting markedly increases the activity of both beta-glucosidase and beta-glucuronidase.<sup>69</sup> Humans with Goucher's Disease are deficient in beta-glucosidase, and this enzyme must be supplemented for these patients. Beta-glucosidase as mentioned above has been found in the membranes of red blood cells but whether this contributes to any significant hydrolysis is obscure.<sup>78</sup>

The inhibition of beta-glucosidase by dietary factors needs additional research but it is known that beta-glucosidase from intestinal microorganisms is inhibited by 1:4 and 1:5 lactones of gluconic acid.<sup>70</sup>

The cleavage of the two D-glucose molecules from amygdalin to yield mandelonitrile is dependent on beta-glucosidase activity, which in turn is related to diet. (Enterococci)

Beta-glucosidase activity is one limiting parameter in amygdalin-based metabolic therapy. The amygdalin which has not been hydrolyzed or metabolized will be excreted intact in the urine. The estimated half-life of amygdalin in plasma is from 3 to 6 hours.

#### RECTAL OR ENEMA ADMINISTRATION OF AMYGDALIN

As pointed out previously, the specific hydrolyzing enzyme Beta-glucosidase reaches its peak concentration in the lower intestine, which results in the cleavage of the two glucose molecules from amygdalin. In addition the pH of the lower intestine is alkaline which will hydrolyze the mandelonitrile to benzaldehyde and hydrogen cyanide.

Enema administration therefore is the most toxic route and should be used with extreme care for the above reasons. Serious side reactions have resulted from less than one gram rectally<sup>87</sup> and at least one death may be attributed to enema administration.

## BETA-GLUCOSIDASE, GLUCOSE

### AND AMYGDALIN

Beta-glucosidase, glucose and amygdalin enhance tumor hyperacidulation through intravenous infusions. The glucose lowers the pH of the cancer cell from a normal 7.3 to 5.7, enhancing glucuronide breakdown, and the beta-glucosidase supplementation enhances the hydrolyzation of the two glucoses from the amygdalin compound, which is the first step in the biosynthesis of Laetrile. In vivo studies show significant tumor regression in carcinosarcomas in 5 to 20 gram tumors.<sup>64</sup>

Before discussing further the biochemical pathway it is necessary to review the detoxification process which occurs in the liver and, to a lesser extent, the kidneys.

### THE FORMATION OF GLUCURONIDES

#### AS A DETOXIFICATION PROCESS

One of the body's primary mechanisms for the removal of certain toxic substances is to couple them with glucuronic acid, hence forming a glucuronide. The glucu-

ronide is ionic because of the free carboxyl group ( $\text{CO}_2\text{H}$ ) and as such is much less able to penetrate a lipid membrane than was the original toxic substance. Glucuronides tend therefore to be biologically inert and are readily eliminated in the urine.<sup>36</sup> It is this glucuronide metabolic pathway which is responsible for the formation of D-l-mandelonitrile glucuronide or laetrile.

In the liver the toxic substance (alcohol or amine), specifically mandelonitrile, is coupled to glucuronic acid by employing the co-factor uridinediphosphoglucuronic acid (UDPGA), through the action of the enzyme, uridine diphosphoglucuronyltransferase (UDPG transferase), with the concurrent formation of uridine diphosphate (UDP). The result is the glucuronide of the toxic substance.<sup>3,4</sup>

The membrane-bound enzyme, UDPG transferase, is unusual in that its active site is masked by lipids.<sup>56</sup> Unless the toxic substance has some degree of solubility in the particular lipids covering the enzyme, the substrate will not contact the active site and glucuronide formation will

not occur regardless of the presence of the co-factor UDPGA.<sup>5</sup>

UDPG transferase is dormant until about the time of birth. One of the functions of this enzyme is to produce the glucuronide of toxic bilirubin, which accounts for the concern at the time of birth over whether this activity is actually underway.<sup>7</sup> The enzyme may become dormant again at any time in adults and in extreme cases results in Gilbert's syndrome, in which there is an almost complete cessation of glucuronide formation.<sup>8</sup>

#### ASPIRIN TEST

A simple clinical test may be made to indicate the degree of activity of UDPG transferase. A gram of aspirin is administered orally and after 24 hours the urine is examined for the presence of the glucuronide of salicylic acid. It has been found that there are wide variations among adults in the ability to form glucuronides.<sup>8</sup> Research is currently underway aimed at developing a simple assay for detection of specific glucuronides.

#### MYRISTIC ACID

It has been shown that the lipid acceptor<sup>9</sup> for the toxic substance in the glucuronidation process exhibits maximum activity when myristic acid is available in the diet.<sup>10</sup> Myristic acid is a 14-carbon saturated fatty acid which apparently is incorporated into the lipid material, hence increasing the activity of UDPG transferase.<sup>11,12</sup> This reality, together with many other necessary dietary factors outlined below, may account in part for the variable activity of this enzyme in adults<sup>10</sup> and the resultant ability to form glucuronide conjugates.

#### OTHER UDPG TRANSFERASE

##### DIETARY FACTORS

Other factors which influence the activity of UDPG transferase are:

1. The enzyme is stimulated by a low-protein diet.<sup>13</sup>
2. Moderate amounts of alcohol stimulate its activity while excessive amounts depress it.<sup>14</sup>



3. Lecithin acts as a stimulant.<sup>6</sup>
4. RNA acts indirectly as a stimulant.<sup>15</sup>
5. Vitamin E acts as a stimulant.<sup>16</sup>
6. Manganese stimulates it indirectly by stabilizing the precursors of the co-factor UDPGA.<sup>17</sup> (Foods containing large amounts of manganese are: certain spices: (cardamom, ginger, cinnamon, clove), the brans: (rice, wheat, buckwheat), certain herbs: (sorrel, dock, dandelion leaf), tea leaves and orange marmelade.<sup>18</sup>
7. The commonly used food preservative BHA almost completely inhibits the enzyme while BHT is without effect.<sup>19</sup>
8. UDPGA may be administered in supplemental amounts.<sup>21</sup>
9. Uridine monophosphate (UMP) may also be supplemented.<sup>22</sup>
10. Excessive use of aspirin should be avoided.<sup>24</sup>
11. Excessive use of chlorpromazine should be avoided.<sup>25</sup>

12. The divalent ions of calcium and magnesium act as stimulants.<sup>26,27</sup>
13. Selenium acts indirectly by preventing lipid membrane modifications.<sup>73,75</sup>

### GLUCURONIC ACID

Glucuronic acid, which is an integral part of the production of glucuronides, is derived from glucose metabolism and is formed by the oxidation of iridine diphosphoglucose in a two-step process. This may shed some light on the fact that individuals with sugar dysfunction problems have a statistically significant higher rate of cancer.

### SELENIUM

Selenium is a component of the enzyme glutathione peroxidase, which breaks down hydrogen peroxide. Hydrogen peroxide breaks down unsaturated fatty acids in bilipid membranes. It may be postulated that increased glucuronidation with selenium supplementation is due to the inhibi-

tion of hydrogen peroxide modification of the lipids surrounding UDPG transferase.<sup>73,75</sup>

### INSULIN

An adequate supply of insulin is essential to maintain fully the capacity of the liver to form glucuronic acid conjugates, or glucuronides. Insulin acts by increasing liver uridine diphosphoglucose (UDP) dehydrogenase activity and thus supplies additional UDPGA for conjugation.<sup>37</sup>

Those who are suspected of having high levels of blood sugar should also undergo testing. Insulin deficiency has been shown to be associated with low levels of UDPGA, as much as a 50% decrease. Those having inadequate insulin levels should be supplemented.<sup>37</sup>

### BIOCHEMICAL PATHWAYS (Continued)

We now return to the biochemical pathway of amygdalin with the realization that mandelonitrile, in fact a secondary alcohol, resulting from the stepwise removal of gentiobiose through beta-glucosidase activity is recognized

as a toxic substance by the detoxification process. In individuals with an adequate detoxification system this results in the synthesis of D-1-mandelonitrile glucuronide, commonly known as laetrile.

Hence, we may say that laetrile is produced primarily in the liver by the detoxification process during amygdalin therapy provided the detoxification system is adequate.

Considering the above-described biochemical chain of events, it is now apparent why it is of the utmost importance for the patient undergoing amygdalin therapy to have a detoxification system which is adequately synthesizing laetrile from the breakdown product of amygdalin.

### LEAKY MEMBRANE

Malignant cells possess what has been termed a "leaky membrane," referring to the outer or plasma membrane of the cell.<sup>20</sup> Small organic molecules readily diffuse across this membrane in a manner not characteristic of normal cells. A second significant difference between malignant and normal cells is the leaky membrane surround-

ing the small cytoplasmic sacs known as lysosomes, which contain a variety of hydrolyzing enzymes. It is known that in malignant cells the lysosomal contents leak into the cytoplasm and thereby make available for cellular activity — among others — the enzyme beta-glucuronidase.<sup>23,28,29</sup>

### MITOCHONDRIA

The mitochondria are subcellular organelles and are the so-called "energy factories" of the cells which receive stored oxygen from myoglobin. Myoglobin consists of a single polypeptide chain and one "heme" group. Myoglobin combines with oxygen released by the red blood cells and transports it to the mitochondria, where the oxygen degenerates into biochemical energy by the combustion of glucose to carbon dioxide and water thereby generating stored energy in the form of ATP (adenosine triphosphate) in the process called "oxidative phosphorylation."

Just how the breakdown of glucose transfers energy to ATP is obscure and controversial. In England, Peter

Mitchell received a Nobel Prize in October, 1978, for his theory of "chemiosmotic coupling," based on a "proton gradient" as a physical mechanism. His theory suggests that protons are transported across the mitochondrion membrane, creating an ion gradient whose potential energy is transferred to ATP.<sup>76</sup>

The transmembrane pH difference (pH of mitochondrion matrix vs. pH of cytoplasm) governs the ionic substrate translocation across the mitochondrial membrane<sup>35</sup> and the swelling of the membrane. The increase in alkalinity is accompanied by mitochondrial swelling resulting in a considerable loss of co-factors and an uncoupling of oxidative phosphorylation. Not only does diet play a role in the shape and function of the mitochondria, but psychological or nervous factors also have a physiological effect on this condition which may account in part for the effects of positive mental attitude. Very little is known about the mechanism controlling these morphological changes within the cell, but they do directly inhibit the exchange-diffusion reactions across the mitochondrial



membrane which in turn have an effect on aerobic and anaerobic balance.<sup>34</sup>

Cytochrome oxidase normally binds molecular oxygen in the same manner as the "heme" group in hemoglobin. The cyanide ion has the ability to displace oxygen from this site, which inhibits enzyme activity.<sup>31,32</sup> If this blockage continues for a sufficient length of time, cell death will result. Moreover, the cytoplasm of malignant cells is more acidic than that of normal cells due to the increased production of lactic acid.<sup>33</sup> In contrast, the mitochondria are somewhat alkaline.<sup>34</sup> The significance of these pH differences is that mandelonitrile will have a tendency to remain intact and not break down in an acid medium of the cytoplasm but will split in the alkaline medium inside the mitochondrion with the resultant release of cyanide and benzaldehyde in the mitochondria. (See previous discussion — Cyanide Cleavage from Mandelonitrile Under Base Conditions.)

An additional influence of diet on amygdalin therapy is that the mitochondria becomes more alkaline and the

cytoplasm becomes more acid during fasting periods or low-protein ingestion.<sup>34</sup>

#### LYSOSOMES — VITAMIN A

The enzyme beta-glucuronidase, which leaks from the lysosomes of cancerous cells, has a pH optimum of 5.2. It is known that glucose administration selectively lowers the pH of tumor cells thereby increasing the effectiveness of this enzyme.<sup>36</sup> Administration of 500,000 units or more of Vitamin A results in an increased leakage of beta-glucuronidase from lysosomes as well as a significant increase in the blood glucose level.<sup>57</sup> The result of megadoses of Vitamin A administration is therefore twofold — it not only causes the liberation in greater quantities of beta-glucuronidase from lysosomes but also indirectly lowers the pH of the cancer cell, thereby increasing the activity of this enzyme.

## D-GLUCARIC ACID

One of the known effective inhibitors of beta-glucuronidase is D-glucaric acid (D-glucosaccharic acid).<sup>58</sup> This acid is normally produced in the liver in small amounts and excreted in the urine. Studies have shown that the amounts produced vary from one individual to another.<sup>59</sup> It has been demonstrated that the administration of phenobarbital and other barbiturates possibly used in cancer therapy greatly increases urinary levels of this metabolite. Other drugs (e.g., progesterone, diphenylhydantoin) also cause a greater production of this powerful inhibitor of beta-glucuronidase<sup>60</sup> and some individuals produce much more of D-glucaric acid than do others.<sup>59</sup> Considerable research is underway concerning this substance and assays have been developed for glucaric acid determination. The presence of this strong inhibitor, which research has shown will penetrate cell membranes,<sup>60</sup> could be a limiting factor in the hydrolysis of laetrile at the malignant lesion, and it is suspected that increased levels of this inhibitor may

account for the wide variation of beta-glucuronidase activity within a given species.<sup>58</sup>

The following drugs stimulate the production of glucaric acid as measured in the urine and should be avoided:<sup>60,61,62</sup>

1. Phenobarbital and other barbiturates
2. Progesterone
3. Diphenylhydantoin (used in the treatment of epilepsy)
4. Contraceptive pills including but not limited to: Ovulen, Orthonovin, Gynovlar, Conoved E

In addition to glucaric acid, which is also found in the pectin-gel of sunflower seeds, the naturally occurring isomer, laevorotatory malic acid found in apples is an effective inhibitor of beta-glucuronidase.<sup>58</sup>

The variation between patients in the concentration of glucaric acid may be a significant factor in amygdalin-based metabolic therapy.

## BETA-GLUCURONIDASE

The enzyme Beta-glucuronidase is capable of splitting the glucuronide, D-1-mandelonitrile-beta-glucuronide, or laetrile, into its components. One of them, mandelonitrile, then spontaneously breaks down under slightly alkaline conditions to benzaldehyde and hydrogen cyanide. As far as is known, this is not an enzyme reaction but is pH dependent in man.<sup>30</sup>

The specificity of toxic cyanide from laetrile for malignant cells lies in the leakage of beta-glucuronidase from the lysosomes of these cells into the cytoplasm as compared to leakage of this enzyme in normal cells.<sup>28</sup> Too, it is known that glucuronides do not enter normal cells and are biologically inert.<sup>36</sup>

Beta-glucuronidase is one of the lysosomal enzymes with a pH optimum of 5.2 and is widely distributed throughout the body with a considerable variation in activity within a given species.

Malignant cells have a considerable increase in beta-glucuronidase activity due to the leaky lysosomal membrane

and the enzyme is present in the serum due to the leakage through plasma-cell membranes.<sup>28</sup>

Increase in beta-glucuronidase leakage from lysosomes can be increased by a factor of 400 measured in blood serum with the injection of 500,000 units of Vitamin "A." In addition, Vitamin A can cause an increase in blood sugar levels in excess of 135 mg%.<sup>57</sup>

Above 10,000 units Vitamin "A" must be taken in the emulsified form in order to avoid toxicity to the liver. Micronic, emulsified, fat soluble vitamins are absorbed by the villi into the lymph ducts and are transported to the systemic circulation, thus bypassing the liver. Highly concentrated emulsified Vitamin A has been given in amounts in excess of a million units daily without liver retention or reported side effects. Some side effects, however, may be encountered, but they are completely reversible.

An integral part of the holistic metabolic therapy is the plasma membrane transport system in the malignant



cell. Enzymes, vitamins, minerals and hormones all play a role in these systems.

From what has been presented it appears that the variable response noted in the treatment of malignancy with amygdalin may result in part from individual differences in the patient's ability to synthesize glucuronides, as well as in the activity of the specific hydrolyzing enzyme, beta-glucuronidase. If this is true the widespread application of a simple clinical test for glucuronide formation and beta-glucuronidase activity in relation to amygdalin response would lead to a statistically significant correlation between these variables.

Those individuals showing a deficiency in glucuronide synthesis or glucuronidase activity would undergo a treatment of metabolic and dietary supplements until normal levels are restored. Amygdalin therapy response will increase when it can be demonstrated that the patient possesses a detoxification system capable of sufficient glucuronide synthesis and with sufficient beta-glucuronidase activity at the malignant site.

## EDTA AND TRYPSIN

It has been shown that cancer cells have a reduced calcium level in the cell bilipid membrane and fewer glycoproteins. EDTA assists in removing a portion of the glycoprotein cell coat of cancer cells by chelation of  $\text{Ca}^{++}$  bridges. In contrast, trypsin produces a deeper enzymatic cleavage that affects the structural integrity of the bilayer lipid cell membrane.<sup>51</sup>

This is corroboration of the empirical evidence of practicing physicians that moderate EDTA chelation therapy improves the patient's response to laetrile-based metabolic therapy. For a more detailed dissertation on chelation therapy, see Protocols for Chelation Therapy, American Academy of Medical Preventics (AAMP).

## DMF

DMF (N,N-Dimethylformamide) has been shown to induce morphological differentiation and reduction of

tumorigenicity in cultured mouse cells (rhabdomyosarcoma cells), as well as in vivo studies with mice.

Properties of cells became more like normal cells rather than malignant cells.<sup>72</sup>

### GERMANIUM

Organogermaniums sesquioxide it is speculated affects tumor diminution because of the ability of the compound to loosely bind oxygen which in turn is carried to the cancer cell, affecting the anaerobic energy process. This compound also has been used as an effective hypertensive agent.<sup>68,71</sup>

### THIOSULFATE - THIOCYANATE

Thiosulfate acts by penetrating the mitochondrial membrane where it furnishes sulfur to rhodanese in the presence of cyanide to produce thiocyanate.

Thiocyanate is a natural hypotensive agent and can be supplemented for the treatment of hypertension at blood serum levels from 8 to 30 mg percent.<sup>75</sup> The normal

thiocyanate level is proportional to the amount of nitrilosidic food — that is, foods containing cyanogenic compounds — in the diet. Those who are accustomed to typical Western eating habits have thiocyanate levels 5 to 8 times lower than those of cultures in which much higher levels of nitrilosides are ingested, a fact which forms the basis for the theory that adequate nitriloside (also designated Vitamin B17) may be the preventive factor, or at least a major factor, in the prevention of cancer and very likely of other conditions.

Thiocyanate is found in maximum concentration in the thyroid where it affects the production of thyroxin, a natural blood pressure regulator.<sup>77</sup> Iodine supplementation may be used to normalize thyroxin in the presence of elevated thiocyanate levels.

It is commonplace to observe a lowering of high blood pressure in patients undergoing amygdalin-based metabolic therapy.

Thiocyanate also is an effective inhibitor of ATPase, an enzyme necessary in the conversion of ATP to ADP in the aerobic glycolysis pathway of cells.<sup>45</sup>

### RHODANESE

It has been stated that one of the decomposition products of mandelonitrile is hydrogen cyanide or its active form, the cyanide ion ( $\text{CN}^-$ ). The detoxification of cyanide is brought about by the enzyme rhodanese, which utilizes thiosulfate to convert toxic cyanide to nontoxic thiocyanate.<sup>38</sup> Rhodanese is found only in the mitochondrion,<sup>39</sup> the principal site of mandelonitrile decomposition. The uptake of anions, including Laetrile, by mitochondria is discussed more fully below.

### HCG

Human chorionic gonadotropin (HCG) is found in cancer cells<sup>63</sup> and during pregnancy. HCG is a powerful inhibitor of rhodanese<sup>40</sup> which allows cyanide liberated from mandelonitrile decomposition to survive conversion

to nontoxic thiocyanate. Thus, cyanide is free to inhibit both the iron-containing enzymes of the respiratory pathway including cytochrome oxidase, as well as inhibit aldehyde oxidase allowing benzaldehyde to effect the glycolytic pathway and pyruvate dehydrogenase effecting the oxidative pathway (to be discussed later).<sup>31,32</sup>

### GLYCOLYSIS

The biochemical pathway from glycogen to lactic acid is known as glycolysis. Under aerobic conditions the immediate precursor of lactate (pyruvate) is further metabolized by the tricarboxylic acid cycle thus preventing an accumulation of lactic acid (Pasteur effect). Under anaerobic conditions (fermentation) the metabolism of pyruvate does not occur due to a biochemical defect in the tricarboxylic acid cycle. Because of the oxygen deficiency lactate accumulates resulting in a lowering of cellular pH (Warburg effect).<sup>33,42</sup>

It is postulated that in cancerous cells the fermentation pathway is converting pyruvate to lactate resulting



from an impaired tricarboxylic acid cycle. This defect drops cellular pH values to as low as 5.7 causing a pH gradient across mitochondrial membranes.<sup>33</sup> The typical mitochondrial pH value of 7.4 may assist in the uptake of mandelonitrile by mitochondria. Mandelonitrile glucuronide (that is laetrile) being an anion (negatively charged) should be incorporated into the mitochondria of cancerous cells at a greater rate than into those of normal cells.<sup>35</sup>

### **PYRUVATE KINASE**

It has been pointed out that there are in the cancerous cell two biochemical pathways related to the utilization of sugar — namely, the respiratory (aerobic) pathway and the so-called alternate pathway or fermentation (anaerobic) one, which results in the production of lactic acid.

Pyruvate kinase is an enzyme which is a determinant in the proportion or balance between these two pathways. An inhibition of pyruvate kinase stimulates the respiratory rate and concurrently decreases the glycolytic rate of the cell. A realization of this effect may be put to practical

use when considering that one of the known inhibitors of pyruvate kinase is the essential amino acid phenylalanine.<sup>42</sup> Incorporation of large amounts of phenylalanine into the diet may swing the balance between the respiration and fermentation pathways away from the fermentation mode.

Certain foods contain larger amounts of this essential amino acid than others — including, in decreasing order, casen (milk protein), wheat gluten, low fat soybean meal and dried brewer's yeast.<sup>43</sup>

### **BENZALDEHYDE**

The presence of the two biochemical pathways of sugar metabolism in cancer cells indicates that the effectiveness of cell damage through cyanide alone is limited. The alternate pathway provides a means whereby the cell may continue to survive even though respiration is inhibited by cyanide.<sup>41</sup> The second of the two decomposition products of mandelonitrile — namely, benzaldehyde — acts to inhibit the alternate pathway, as will be discussed. Thus, each of the two products resulting from

the breakdown of amygdalin acts predominantly on one of the two biochemical pathways necessary for cell survival.

Research has shown that there is a toxic, synergistic effect between cyanide and benzaldehyde.<sup>44</sup>

A critical step in glycolysis is the conversion of ATP to ADP by mitochondrial ATPases.<sup>45</sup> Oxidation cannot proceed without ADP thus linking the two pathways (aerobic and anaerobic) together. Benzaldehyde has been shown to inhibit both the sodium, potassium and magnesium ATPases.<sup>43</sup> The amino acid cysteine protects ATPase from inhibition by aldehydes, including benzaldehyde.<sup>46</sup> Since cysteine is one of the sulfur-containing amino acids this result implies that excessive sulfur in the diet may impair the inhibition of ATPase by benzaldehyde.

#### THIOCYANATE VERSUS ATPase

It has also been shown that the thiocyanate ion resulting from detoxification of cyanide also inhibits ATPase.<sup>47</sup>

#### ANALGESIC EFFECT

It has long been known that benzaldehyde has an analgesic effect in the treatment of cancer patients. This effect is caused by changes in the permeability of nerve membranes to sodium and potassium. There is an increase in membrane conduction to potassium and a concurrent decrease in permeability to sodium relative to potassium, which in turn inhibits the firing of the neuron.<sup>48</sup>

Both benzaldehyde and its metabolite, benzoic acid, increase nerve membrane conduction to potassium ( $K^+$ ) and decrease the permeability to sodium  $Na^+$  relative to potassium, inhibiting nerve activity.

#### ALDEHYDE OXIDASE

Human liver aldehyde oxidase has the ability to oxidize aldehydes (including benzaldehyde) to the corresponding carboxylic acids thus reducing the effectiveness of benzaldehyde inhibition of ATPase. However, it has been shown that cyanide is an inhibitor of aldehyde oxidase,

thus preserving to some degree the effectiveness of benzaldehyde as an analgesic and its inhibition of ATPase.<sup>49</sup>

### **PYRUVATE DEHYDROGENASE**

The conversion of pyruvate to a form required for entering the tricarboxylic acid cycle involves the pyruvate dehydrogenase complex, a set of closely related enzymes. This part of the oxidative pathway is also inhibited by benzaldehyde.<sup>50</sup>

### **WHY AMYGDALIN THERAPY MAY FAIL**

Variation in cancer therapy with amygdalin results from several basic causes:

1. The cleavage of the two glucose units from amygdalin to yield mandelonitrile is dependent on beta-glucosidase activity — which, as we have seen, is related to specific inhibitors and the intestinal flora which in turn is related to diet.
2. An impaired detoxification system results in lowered synthesis of mandelonitrile glucuronide (laetrile) from

amygdalin by the body. In cancer of the liver this system may be extremely deficient because the major detoxification processes reside in this organ. As pointed out before, efficient operation of the detoxification system is certainly diet-related from many standpoints. Among these are the presence of appropriate minerals (Ca, Mg, Mn) and the absence of heavy metals which may inhibit enzyme activity (Pb, Ba, Hg).

3. The plasma membrane (or outer membrane) of cancerous cells is covered with a glycoprotein coat which may in some tumors impair the uptake of glucuronide. Remember that an integral part of metabolic therapy involves the active transport systems into malignant cells, and that the entire dietary universe — enzymes, vitamins, minerals, hormones — all play roles in this.
4. Glucuronides are normally excreted in the urine, thereby limiting the time of effective incorporation into tumor cells. Loss of laetrile through this route has been controlled through the use of drugs causing



temporary blockage of kidney function. An estimate of the half-life of laetrile in the blood is from three to six hours.<sup>84</sup>

5. The condition of the intestinal flora affects the production of large amounts of beta-glucosidase and beta-glucuronidase.
6. Inhibitors of beta-glucosidase and beta-glucuronidase may play an important role in amygdalin based metabolic therapy.
7. Psychological effects also play an important role in the holistic metabolic treatment program.

## TREATMENT CONSIDERATION

### DIET AND FOOD SUPPLEMENTS:

Low fat and animal protein

Average to low sulfur (few eggs)

Peach kernel oil (probably also apricot kernel oil)

—source of myristic acid

Pollen-source of myristic acid

Lecithin

UDPGA (not available in the USA)

RNA (ribonucleic acid, usually from yeast)

Supplemental Calcium, Magnesium and other minerals

S.O.D. - superoxide dismutase

### Foods High in Manganese:

Bran (rice, wheat, buckwheat)

Spices (cardamom, ginger, cinnamon, cloves)

Herbs (sorrel, dock, dandelion leaf)

Orange marmalade

### Foods High in Phenylalanine:

Casein (milk protein)

Wheat Gluten

Low fat soybean meal

Dried brewer's yeast

AVOID:

BHA — butylated hydroxy anisole (an antioxidant food preservative found in margarine and other foods)

Excessive Alcohol

Excessive Aspirin

Certain female contraceptives (drug type)

Certain other drugs including chlorpromazine, phenobarbital and other barbituates, diphenylhydantoin, progesterone

Excessive apples

Excessive sulfur-containing foods (eggs)

ADDITIONAL TREATMENT:

EDTA Therapy

Megavitamin dosages of emulsified vitamins A and E

Megavitamin dosages of vitamin C

Occasional fasting

Test for the patient's ability to produce glucuronides

Test for the patient's ability to hydrolyze amygdalin

Test for the patient's activity of specific inhibitors of glucuronidase and glucosidase

Selenium

Germanium sesquioxide

Enzyme supplements

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## GLOSSARY

(Definitions Applicable to the Usage in this Text)

**Adaptagen** — A non-specific immune stimulant.

**Amine** — An organic substance containing saturated nitrogen.

**Aldehyde oxidase** — An enzyme found in the liver which converts aldehyde to the corresponding carboxylic acid (benzaldehyde to benzoic acid). Inhibited by cyanide.

**Amygdalin** — A disaccharide derivative of mandelonitrile consisting of benzaldehyde cyanohydrin coupled to a linear chain of two D-glucose residues (gentiobiose).

**ATP (adenosine triphosphate)** — A phosphorylated derivative of the nucleic acid (RNA, DNA) component adenosine, containing the high energy triphosphate linkage.

**ATPase** — An enzyme which cleaves one phosphate group from ATP, resulting in the diphosphorylated derivative ADP.

**Benzaldehyde** — An oxidation product of benzyl alcohol. The simplest aromatic aldehyde ( $C_6H_5CHO$ ). Oxidized to benzoic acid by aldehyde oxidase. An analgesic and specific enzyme inhibitor.

**Benzoic Acid** — The simplest aromatic Carboxylic acid ( $C_6H_5CO_2H$ ). Results from oxidation of benzaldehyde by aldehyde oxidase. An analgesic.

**Beta-Glucosidase** — An enzyme found in most all tissues which cleaves terminal D-glucose from polysaccharides or polysaccharide derivatives including amygdalin.

**Beta-Glucuronidase** — An enzyme found in lysosomes which is capable of cleaving glucuronides including laetrile.

G-1

**Biologicals** — A European term describing adaptagens.

**Cyanide** — An organic grouping consisting of one carbon and one nitrogen atom, having a unit negative charge.

**Cysteine** — A sulfur-containing amino acid which bears the sulfhydryl group (-SH). Cysteine protects ATPase inhibition from aldehydes including benzaldehyde.

**Cytochrome oxidase** — An enzyme found in mitochondria related to the utilization of oxygen in the formation of water and heat. A part of the electron transport system.

**Divalent ion** — An ion having a charge of two (2).

**Dextro isomer (+)(S)** — A substance capable of rotating polarized light clockwise.

**D Glucuronic Acid** — Produced by a two step oxidative process from D Glucose. A monocarboxylic anion. The saccharide portion of laetrile.

**DMF (dimethylformamide)** — An organic solvent which is the dimethyl amid of formic acid having the formula  $\text{HC(O)N(CH}_3)_2$ . Recently shown to have an effect on cancer cell differentiation.

**DMSO (dimethylsulfoxide)** — An organic solvent which dissolves difficultly soluble substances. Capable of penetrating cellular membranes (a carrier solvent).

**EDTA (Ethylenediaminetetraacetic acid)** — An organic substance capable of chelating or solubilizing calcium and other divalent ions.

**Ehrlich ascites tumor cells** — A particular type of cancerous cell much used in research characterized by a high glycolytic rate and high contact inhibition.

G-2

**Enantiomers** — The specific stereoisomers that are mirror images due to racemization of all the optically active centers — not applicable to amygdalin or laetrile.

**Electron transport system** — A biochemical process concerned with a series of cytochromes related to the utilization of oxygen. Takes place in the mitochondria.

**Epimers** — Specific stereoisomers that are characterized by racemization of a part of the optically active centers, but not all the optically active centers. Amygdalin and laetrile exhibit epimerization in the presence of hydroxyl groups or basic medium.

**Estrogen** — A steroid hormone that induces estrus.

**Glucuronic acid** — A powerful inhibitor of beta-glucuronidase produced in small amounts in the liver of healthy individuals. Excessive activity will interfere with laetrile metabolism.

**Glucuronides** — Organic substances consisting of glucuronic acid coupled to an alcohol or an amine.

**Glycolysis** — The metabolic pathway from glycogen to lactic acid, representing the failure to metabolize pyruvic acid through the tricarboxylic acid cycle.

**HCG (Human chorionic gonadotrophin)** — A glyco-protein consisting of two peptide chains, alpha and beta, found in cancer patients and during pregnancy. Inhibits the enzyme rhodanese.

**Hydrogen cyanide (HCN)** — A grouping consisting of a cyanide ion plus a proton — a non-charged molecule.

**Insulin** — A protein hormone acting on the pancreas relating to the metabolism of sugar.

G-3

**Lactate dehydrogenase** — An enzyme which converts lactic acid to pyruvic acid or the reverse. An integral part of the glycolysis pathway.

**Lactic acid** — The metabolic product resulting from the hydrogenation of pyruvic acid.

**Lactic Dehydrogenase** — An enzyme which converts lactate to pyruvate and the reverse action of pyruvate to lactate (anaerobic pathway).

**Laetrile** — A derivative of mandelonitrile consisting of benzaldehyde cyanohydrin coupled to glucuronic acid.

**Levo isomer (-)(R)** — A substance capable of rotating polarized light counterclockwise.

**LD<sub>50</sub> (Lethal dose fifty)** — The amount of a substance which is expected to kill 50% of a population of experimental animals.

**Lysosome** — A sub-cellular component (organelle) found in the cytoplasm consisting of a membranous sac enclosing various enzymes.

**Mandelonitrile C<sub>6</sub>H<sub>5</sub>CH (OH) CN** — Benzaldehyde cyanohydrin resulting from the hydrolysis of amygdalin and other cynogenic glycosides. A component of laetrile.

**Mitochondrion** — A small subcellular component which utilizes molecular oxygen in the production of ATP. Also called the "energy factory of the cell."

**Myristic acid** — a 14-carbon saturated fatty acid which optimally stimulates the enzyme responsible for synthesizing glucuronides (UDPG transferase).

**Optical activity** — The rotation of polarized light by a substance containing asymmetric carbon centers.

G-4

**Optical isomers** — An organic substance containing one or more asymmetric carbon centers (a carbon bearing four different groups) resulting in optical activity.

**Oxidative phosphorylation** — A biochemical process which applies phosphate groups to the substances of the tricarboxylic acid cycle resulting in the production of ATP.

**Pasteur effect** — The failure of lactic acid to accumulate in a cell due to the metabolism of its precursor pyruvic acid by the tricarboxylic acid cycle.

**Phenylalanine** — One of the essential amino acids. Inhibits pyruvate kinase.

**Prunasin** — A monosaccharide derivative of mandelonitrile consisting of benzaldehyde cyanohydrin coupled to a D-Glucose residue.

**Pyrophosphate** — Two phosphate groups coupled together.

**Pyruvic acid** — An intermediate preceeding the tricarboxylic acid cycle and/or lactic acid formation.

**Pyruvate dehydrogenase complex** — Enzymes which convert pyruvate to a form acceptable to the citric acid or tricarboxylic acid cycle. Inhibited by benzaldehyde.

**Pyruvate kinase** — An enzyme responsible for the production of pyruvic acid thereby controlling the balance between the respiration and glycolytic pathways. Inhibited by phenylalanine.

**Racemic modification** — A mixture of equal parts of enantiomers which is optically neutral. The specific isomeric configuration characterized by mirror image configurations. Not applicable to amygdalin or laetrile.

**Rhodanese** — An enzyme found only in mitochondria capable of converting toxic cyanide ion to non-toxic thiocyanate ion.

G-5



**Stereoisomer** — A compound that has the same number and kind of atoms as another compound, and of similar structure, but of different arrangements of atoms in space.

**TDL<sub>20</sub>** (Toxic Dose low) — The lowest amount of a substance which will produce a toxic response of any kind.

**Thiocyanate** — A negative ion formed by coupling one atom of sulfur to the cyanide ion,  $\text{CN}^-$ . Has the formula  $\text{SCN}^-$ .

**Thiosulphate** — A negative ion formed by replacing one oxygen atom of the sulphate ion,  $\text{SO}_4^{2-}$ , with sulfur. Has the formula  $\text{S}_2\text{O}_3^{2-}$ .

**Thyroxine** — A hormone containing iodine biosynthesized in the thyroid which regulates metabolism and blood pressure.

**Tricarboxylic acid** — An organic acid containing three carboxy groups ( $\text{CO}_2\text{H}$ ).

**Tricarboxylic Acid cycle (citric acid cycle)** — A cyclic set of biochemical transformations resulting in energy formation in the form of ATP.

**UDPGA (Uridine diphosphoglucuronic acid)** — A cofactor required in the formation of glucuronides by transferase. Consists of uridine coupled to glucuronic acid through pyrophosphate.

**UDP (Glucose** — Precursor of UDPGA.

**UDPG transferase** — Uridine diphosphoglucuronyltransferase. An enzyme found principally in the liver which forms the glucuronides of toxic substances including alcohols and amines. Responsible for the formation of laetrile from mandelonitrile, the breakdown product of amygdalin.

G-6

A-70

**UDP Uridine diphosphate)** — A byproduct in the formation of glucuronide by UDPG transferase. A phosphorylated derivative of the nucleic acid component, uridine.

**Warburg effect** — The excessive production of lactate in cancer cells from a failure to convert pyruvate via the tricarboxylic acid cycle.

G-7

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Supreme Court, U. S.

E I L E D

APR 5 1979

MICHAEL ROBAK, JR., CLERK

IN THE  
**Supreme Court of the United States**

October Term 1978

**No. 78-605**

THE UNITED STATES OF AMERICA, et al.,  
*Petitioners,*

*v.*

GLEN L. RUTHERFORD, et al.,  
*Respondents.*

**BRIEF OF AMICUS CURIAE  
AMERICAN ACADEMY OF MEDICAL PREVENTICS  
IN SUPPORT OF RESPONDENTS**

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IN THE SUPREME COURT OF THE UNITED STATES

OCTOBER TERM 1978

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THE UNITED STATES OF AMERICA, ET. AL.,

PETITIONERS

V.

GLEN L. RUTHERFORD, ET. AL.,

RESPONDENTS

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BRIEF OF AMICUS CURIAE  
AMERICAN ACADEMY OF MEDICAL PREVENTICS  
IN SUPPORT OF RESPONDENTS

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By consent of petitioner and respondent American Academy of Medical Preventics files this brief as Amicus Curiae.

INTEREST OF AMICUS CURIAE

The American Academy of Medical Preventics is a nationwide group of physicians with 133 paid members. The Academy's purpose is the promotion and dissemination of information to physicians and the public regarding alternative methods of essentially nontoxic therapies for the treatment of chronic and degenerative disease.

The Academy is particularly interested in the issues involved in this case regarding the constitutional right of an



informed consenting patient to receive essentially nontoxic therapies from a licensed physician, and whether the flat prohibition of such therapies prior to State approval is reasonably related to the preservation and protection of the public health.

The parties herein are properly concerned with establishing their positions on the facts of the case. The Academy, however, respectfully requests that the Court, in considering the specific issues in the case, also give consideration to the broader aspects of the issues.

#### SUMMARY OF ARGUMENT

That class of cancer victims who desire to obtain and use Laetrile in a program of nutritional therapy is protected by constitutional guarantees of privacy and personal liberty. Since cancer victims cannot meaningfully exercise this right in isolation, the constitutional protection accorded cancer victims' right to utilize Laetrile extends to physicians willing to administer Laetrile. State interference with informed consenting cancer victims' constitutionally protected right to obtain and use Laetrile administered by a licensed physician is not necessary to further any substantial or compelling State interest. State interests in preventing delay of State sanctioned treatments, preventing fraudulent and deceptive practices, and providing information about State sanctioned treatments are not accomplished by a complete ban on Laetrile. These State interests are certainly not accomplished in the least restrictive way to prevent infringement on cancer victims' constitutional right of privacy and personal

liberty.

21 U.S.C. 355, as applied, prohibits all cancer victims from obtaining Laetrile. This includes those cancer victims diagnosed as terminal or too frail for State sanctioned treatments by competent medical advisors, cancer victims who seek to supplement State sanctioned treatments with nutritional treatment that includes Laetrile, and cancer victims who have rejected State sanctioned treatments after receiving competent medical advice. The law, as applied, requires forced State sanctioned treatments or nothing at all. The law is brutal and offensive to human dignity as well as cruel and inhuman. A law that isolates cancer victims from a licensed physician is certainly not reasonably related to the preservation and protection of the public health.

ARGUMENT

I

Federal Food, Drug And Cosmetic Act Section 505, 21 U.S.C. 355, And Its Application, Unlawfully Precludes Cancer Victims From Exercising Their Constitutional Rights To Obtain And Use Laetrile In Violation Of United States Constitution Amendments I, IV, V, IX, And XIV.

A. That class of cancer victims who desire to obtain and use Laetrile in a program of nutritional therapy is protected by Constitutional guarantees of privacy and personal liberty.

Long before our Bill of Rights or our political parties or the State's concern with the nature of treatment received by cancer victims, a zone of privacy, innate in every human being, has existed. The fundamental nature of this right derives from the very nature of man.

In perhaps the best known dissent in American jurisprudence, Justice Brandeis recognized the fundamental nature of the "right to be let alone" in Olmstead v. United States, 277 U.S. 438 (1928), where he stated at page 478:

The makers of our Constitution undertook to secure conditions favorable to the pursuit of happiness. They recognized the significance of man's spiritual nature, of his feelings and of his intellect. They knew that only a part of the pain, pleasure, and satisfaction of life are to be found in material things. They sought to protect Americans in their

beliefs, their thoughts, their emotions, and their sensations. They conferred, as against the government, the right to be let alone--the most comprehensive of rights and the right most valued by civilized men. To protect that right, every unjustifiable intrusion by the government upon the privacy of the individual, whatever the means employed, must be deemed a violation ....

Without substantive values beyond those of assuring the fair implementation of the State's own positive decisions, the Constitution could protect little beyond the entitlements government chose to confer. The thesis of substantive values beyond enumerated ones in the Bill of Rights was recognized in Poe v. Ullman, 367 U.S. 497 (1961) by Justice Harlan as a "rational continuum" where he stated at page 543:

The full scope of the liberty guaranteed by the Due Process Clause cannot be found in or limited by the precise terms of the specific guarantees elsewhere provided in the Constitution. This 'liberty' is not a series of isolated points pricked out in terms of the taking of property; the freedom of speech, press, and religion; the unreasonable searches and seizures; and so on. It is a rational continuum which, broadly speaking, includes a freedom from all substantial arbitrary impositions and purposeless restraints, ... and which also recognizes, ... that certain interests require particu-

larly careful scrutiny of the state needs asserted to justify their abridgement.

The Court has found a constitutional right to privacy or personal liberty in several constitutional provisions. A privacy right has been held implicit in the "Penumbra" of the specific guarantees of the 1st, 4th, and 5th Amendments of the Constitution, Griswold v. Connecticut, 381 U.S. 479 (1965); the 9th Amendment's reservation of certain rights to the people, Griswold v. Connecticut, *supra*, (Goldberg, J., concurring); and the 14th Amendment's guarantee of liberty, Roe v. Wade, 410 U.S. 113 (1973).

Although these rights are not specifically enumerated, there are certain areas of individual freedom that are constitutionally protected from government intrusion, and these rights include many different individual activities. The outer limits of the right of privacy and personal liberty have not yet been determined, but this Court has made it clear that unjustified government interference with personal decisions relating to marriage, Loving v. Virginia, 388 U.S. 1, 12 (1967); procreation, Skinner v. Oklahoma, 316 U.S. 535, 541-42 (1942); contraception, Griswold v. Connecticut, 381 U.S. 479 (1965); and child rearing and education, Meyer v. Nebraska, 262 U.S. 390 (1923), Pierce v. Society of Sisters, 268 U.S. 510 (1925); violate this concept.

Perhaps the Court's most comprehensive attempt thus far to define the constitutional right of privacy came in Whalen v. Roe, 429 U.S. 589, 599-600 (1977) where, writing for a unanimous Court,

Justice Stevens suggested that the right encompassed something beyond the least common denominator of the Court's prior decisions with respect to marital choice, procreation, contraception, child rearing and education, and in fact embraced both a general "individual interest in avoiding disclosure of personal matters" and a similarly general, but nonetheless distinct, "interest in independence in making certain kinds of important decisions."

The very core of personal freedom includes the right to control and make decisions about essentially personal affairs. Such decisions have a profound effect on the individual and a negligible effect on society at large.

As the State seeks to apply Section 505, 21 U.S.C. 355, cancer victims are prohibited from obtaining Laetrile from a licensed physician and are permitted to choose only State sanctioned treatments of surgery, radiation therapy, or various forms of chemotherapy. Cancer victims are prevented from making their own personal and intimate decisions with respect to life and death and their own bodies before their lives are consumed by the cancer.

Many cancer victims who are competent and responsible adults seek the right to use a simple and harmless food substance known as "Laetrile," or "amygdalin," or "vitamin B-17," for its subjective effects in relieving them of Cachexia, the horrible physical wasting away of the body which accompanies the cancer, and for other effects that it may possibly have in relieving them of their cancer. They seek to use Laetrile not only for its possible benefits but



for its known benefits. While cancer victims cannot be certain that Laetrile will cure or control cancer, they do know, based upon personal experience, that it provides relief from the terrible pain, depression, and weight loss which mark the progression of their disease. Although such "anecdotal" evidence is condemned by the scientific establishment as "unscientific," courts have historically placed primary reliance on sworn testimony in resolving serious and important disputes.

Because of personal experience, contacts with other cancer patients treated with Laetrile, and a wide variety of literature and other types of information which they have encountered in their attempts to learn more about the disease which threatens their lives, many cancer victims have acquired a conscientious personal conviction that there is substantial validity to a concept of disease and health care which has arisen within the medical and scientific professions in recent years and which is generally known as "metabolic" or "nutritional" therapy.

This conviction is that the metabolic processes of the human body, when functioning properly, include highly sophisticated and effective immunity defenses against cancer; that cancer can only occur and spread when the normal human metabolic processes are not functioning properly; and that the correction of a metabolic imbalance or deficiency in the body may result in the elimination or control of cancer by the body's natural immunity defenses.

Although it is an authorized form of practice under state physicians and sur-

geons certificates, and although it is practiced by a substantial number of physicians within the United States, metabolic therapy is not accepted or recognized by the American Medical Association. However, recent developments indicate that conventional practitioners are now beginning to recognize the value of nutrition in cancer treatment as well as the acute lack of government funds allocated for research in this area. (See U.S. Congress. Senate. Committee on Agriculture, Subcommittee on Nutrition, Nutrition and Cancer Research, Hearings 95th Cong., 2d Sess., June 12 and 13, 1978).

Although a substantial number of physicians and scientists as indicated in Note 9 of the District Court's opinion believe that programs of nutritional therapy which utilize Laetrile might be effective in controlling the symptoms of, or curing cancer, such treatments are highly unconventional. Nutritional therapy in general and the use of Laetrile in particular, are officially regarded by the National Cancer Institute to be of no value whatsoever in controlling or curing cancer.

Cancer victims, of course, could very well be wrong in believing that Laetrile or nutritional therapy may save or prolong their lives. However, the "right to be let alone" is not limited in its recognition to any single segment of the political, economic, or social thought spectrum. In commenting upon Justice Brandeis' most valued of rights, that right to be let alone, new Chief Justice Burger, in his dissent in Application of President and Directors of Georgetown Col., 331 F. 2d 1010 (Dist. of Columbia

1964) stated at page 1017:

Nothing in this utterance suggests that Justice Brandeis thought an individual possessed these rights only as to sensible beliefs, valid thoughts, reasonable emotions, or well-founded sensations. I suggest he intended to include a great many foolish, unreasonable and even absurd ideas which do not conform, such as refusing medical treatment even at great risk.

Cancer victims may also be right. There is substantial support for their beliefs in the efficacy of Laetrile contained in the record below.

The question presented, however, is not whether Laetrile can cure or control cancer. In all probability, the question of whether Laetrile is effective will not be decisively settled within the medical and scientific professions for many years to come.

The issue is human liberty. The question is whether an informed cancer victim can be limited in choice of treatment received from a state licensed physician to State sanctioned alternatives.

As the State would apply Section 505, 21 U.S.C. 355, the State makes the ultimate and final decision for the individual cancer victim and denies an otherwise harmless, but controversial treatment, which cancer victims individually, having weighed the possible risks and benefits, believe might save or prolong their lives.

All of these facts are known to many cancer victims who nevertheless believe that there is a substantial possibility

that a program of nutritional therapy which includes therapeutic doses of Laetrile will result in their cancer being controlled or cured and their lives substantially prolonged. Their use of Laetrile in the past has resulted in significant subjective improvement in their physical deterioration.

They have decided to pursue a course of treatment which has had a demonstrated effect on the symptoms of their disease and have decided to pursue an unconventional course of treatment which might be effective rather than resign themselves to a slow, painful and certain death.

The decisions were subjective, non-medical ones based on intimate and intensely personal considerations which only individual cancer victims can properly evaluate and weigh. This is the right to make what is for them the most important and intensely personal decisions of their lives.

The decision concerns their personal health, their human dignity, and, for some, their very survival. It is a decision which, in the final analysis, is based not upon scientific or objective criteria which can be applied to society as a whole, but rather upon their deepest and most intimate personal concepts of their own lives, their death, their own self-worth, their families and their personal dignity. For all of them, in varying degrees, and for diverse reasons, a significant element in making this decision is their own personal concepts of health and medicine; whether based upon religious tenets or upon personal beliefs as to the nature of human life, the decision involves the extent to which

and under what circumstances one will permit chemicals to enter his body, or a surgeon to remove part of his body. It is difficult to imagine a personal right which is more fundamental and more clearly within the protection of constitutional guarantees of privacy and personal liberty than the right of cancer victims to make this decision.

Long before it was accorded constitutional protection, the basic nature of an individual's right to make decisions concerning his health was recognized by the courts. Justice Cardozo held in Schloendorff v. Society of New York Hospital, 105 N.E. 92 (1914) that a physician who performs an operation without the consent of the patient commits an assault and stated at page 93:

Every human being of adult years and sound mind has a right to determine what shall be done with his own body ....

Under the "informed consent" rule, courts have consistently recognized that even where an individual consciously entrusts his care to a licensed physician having superior medical knowledge, the physician may not deprive the patient of the right to weigh the risks inherent in various courses of treatment and make the final decision. (See Cobbs v. Grant, 8 Cal. 3d 229, 243, 104 Cal. Rptr. 505 (1972); Patients Bill of Rights, Medical Ethics and Legal Liability, 337 (1976); Physician Liability for Adverse Drug Reactions, R. Carleton, Medical Technique Quarterly 184, 195 (Fall 1977).

The right of individuals to make their own informed decisions with the advice

of their own physicians involves a degree of risk-taking. The widespread national opposition to the proposed saccharin ban by the FDA in 1977 by people who preferred running some imperfectly known risk of cancer to a total ban of the substance, resulted in the government almost immediately proposing to make saccharin available as a non-prescription drug. This converted the impact of the chemical's regulation from a serious deprivation to a mild if irritating inconvenience. (See Plans to Ban Saccharin Use Announced by FDA, Food Drug Cos. L. Rep. (CCH) section 41856 (1977) and Saccharin Ban Prompts New Look at Anti-Cancer Clause, id, section 41868 (1977).

Courts have held that constitutional guarantees of privacy includes medical decisions that involve protection from risks of death. In People v. Belous, 71 Cal. 2d 954, 963, 80 Cal. Rptr 354 (1969), the California Supreme Court in protecting the women's abortion decision based their holding partly on the women's right to life since childbirth involves risks of death. Courts have also held that constitutional guarantees of privacy include the right to select a course of treatment which may result in death. In Matter of Quinlan, 355 A. 2d 647 (1976), the New Jersey Supreme Court held that a comatose accident victim, through her family, could terminate extraordinary life-saving measures even though it would probably result in death. Concerning the state's interests in preservation of human health and life, the Court said at page 663:

We have no hesitancy in deciding,



in the instant diametrically opposite case, that no external compelling interest of the State could compel Karen to endure the unendurable, ....

Courts have also held that the state has no power to order life-saving blood transfusions where the patient is opposed to such treatments on the basis of deeply held personal convictions of a religious nature. Erickson v. Dilgard, 252 N.Y.S. 2d 705, 706 (1962).

As the District Court discussed below in note 25, the decision to use Laetrile is by no means indicative of suicidal tendencies and State sanctioned cancer treatments are both oppressive and dangerous. (See New York State Journal of Medicine, 554 (March 1971) where Drs. T. Nemoto and T. Dao, speaking about 5-Flurouracil, a chemotherapeutic agent, said: "Of 133 patients receiving F-5U, 17, or 13%, demonstrated objective regression (of the tumor) ... thirteen patients, or 10% died as a result of F-5U toxicity".).

In Olmstead v. United States, 277 U.S. 438 (1928), Justice Brandeis recognized that it is improper for the State to act solely to protect its citizens for their "own good" where he stated at page 479:

Experience should teach us to be most on our guard to protect liberty when the government's purposes are beneficent. Men born to freedom are naturally alert to repel invasion of their liberty by evil-minded rulers. The greatest dangers to liberty lurk in insidious encroachment by men of zeal, well-

meaning but without understanding.

In People v. Fries, 42 Ill. 2d 446, 250 N.E. 2d 149 (1969), the Illinois Supreme Court also recognized this premise where they held that state's motorcycle helmet law invalid.

Roe v. Wade, 410 U.S. 113 (1973), dealt specifically with the right to determine one's own medical treatment. This Court made it clear that the right protected was the right of the individual to make important medical decisions relating to her physical and mental health where it stated at page 153:

The detriment that the State would impose upon the pregnant women by denying this choice altogether is apparent. Specific and direct harm medically diagnosable even in early pregnancy may be involved. Maternity, or additional offspring, may force upon the women a distressful life and future. Psychological harm may be imminent. Mental and physical health may be taxed by child care.

In Doe v. Bolton, 410 U.S. 179, 213, 219-20 (1973), Justice Douglas in his concurring opinion recognized that "the freedom to care for one's health and person" comes within the purview of the right of privacy; "the right of privacy has no more conspicuous place than in the physician-patient relationship ..."; and "the right to seek advice on one's health and the right to place reliance on the physician of one's choice are basic."

It is beyond question, whether one

agrees or disagrees with those seeking nutritional therapy that includes Laetrile, that their decisions are to try to survive. For some the decision has been to go forward with orthodox cancer therapy and to supplement that therapy with nutritional therapy. For others, who are not willing to undergo or to continue orthodox therapy, for their own personal reasons, nutritional therapy may be their only hope.

Moreover, aside from a potential benefit cancer victims may receive in curing or controlling their disease, their right to life includes the right to spend the remainder of their lives as productively and fully rewarding as possible. Even if it could be conclusively demonstrated that Laetrile is completely ineffective in curing or controlling cancer, their decision would nevertheless be entitled to the protection of constitutional guarantees of privacy and personal liberty because of Laetrile's effect on the terrible symptoms of cancer.

This right to select a particular course of treatment from a licensed physician, otherwise harmless, which may prolong their lives, or at least will allow them to spend the remainder of their lives in dignity, cannot be conditioned on a showing that their ultimate decision is medically or scientifically justified or even that it is reasonable. That determination is uniquely within the province of the individual cancer victim. It is the right to make the decision--the right to weigh the possible benefits, the risks and the expense of a program of nutritional therapy in light of intimate personal feelings and objectives--which is protected by constitutional

guarantees of privacy and personal liberty.

B. The constitutional protection accorded cancer victims' right to utilize Laetrile in a program of nutritional therapy extends to physicians willing to administer Laetrile.

The fundamental right of cancer victims to pursue a course of nutritional therapy is a right which they cannot meaningfully exercise in isolation. The right is not merely a right to use Laetrile, but a right to use Laetrile as an integral part of a program of nutritional therapy carefully worked out by an expert in the area of human nutrition and tailored to suit their individual needs. The therapy often involves the injection of Laetrile in prescribed doses and at prescribed time intervals in conjunction with the administration of other beneficial nutrients.

With respect to the licensed physician's right to freedom to treat, to minister to the sick, the Court in Whalen v. Roe, 429 U.S. 589, 604 (1977) said that "the doctors' claim is derivative from, and therefore no stronger than, the patients." Further, the Court has recognized that the right to make important decisions pertaining to one's health includes the right to obtain the means to implement these decisions. State actions that limit access to the means of effectuating a protected decision are subject to the same strict scrutiny as are state actions that prohibit the decision entirely. Carey v. Population Services International, 431 U.S. 678, 688 (1977); Doe v. Bolton, 410 U.S. 179 (1973); Planned Parenthood of Central Missouri v. Danforth,

428 U.S. 52 (1976).

In Doe v. Bolton, 410 U.S. 179 (1973), this Court invalidated statutory restrictions that infringed upon the right of the patient to receive the benefit of the judgment of the physician of her choice where the Court stated at page 197:

The women's right to receive medical care in accordance with her licensed physician's best judgment and the physician's right to administer it are substantially limited by this statutorily imposed overview.

This Court also discussed the right of an individual to choice of treatment with the advice of the individual's physician in Whalen v. Roe, 429 U.S. 589 (1977) where it stated at page 603:

Nor can it be said that any individual has been deprived of the right to decide independently, with the advice of his physician, to acquire and use needed medication ... Within dosage limits which appellees do not challenge, the decision to prescribe, or to use, is left entirely to the physician and the patient.

In Roe v. Wade, 410 U.S. 113 (1973), this Court specifically upheld the right of the physician to administer medical treatment according to the physician's professional judgment, in consultation with his patient, until there is compelling justification for state inter-

vention. At least until the medical treatment sought to be prohibited is more dangerous than the government sanctioned alternatives, the constitutional right of privacy protects the one seeking treatment and the physician who offers that treatment. Concerning termination of pregnancy during the first trimester, Justice Blackmun speaking for the Court stated at page 163:

... the attending physician in consultation with his patient, is free to determine, without regulation by the State, that, in his medical judgment, the patient's pregnancy should be terminated.

The right of an informed consenting patient to choose unorthodox modalities not yet approved by the State from a licensed physician is within the constitutional protections of privacy and personal liberty. This is certainly compatible with: (1) requiring that certain drugs be available to the public on prescription from a licensed doctor; (2) Compulsory vaccination in which harm to others is readily foreseeable, Jacobson v. Massachusetts, 197 U.S. 11 (1905); and (3) recognition of a compelling state interest in the health of a prospective mother at approximately the end of the first trimester of pregnancy, Roe v. Wade, 410 U.S. 113 (1973).

History, reason and experience supports this premise. Medical progress has been made by physicians with the vision and courage to use alternatives to orthodox modalities and procedures. (See 109 Cong. Rec. 14499 in which Senators Lister Hill and Paul Douglas dis-



cuss the persecution of such great medical innovators as Lister, Pasteur, Semmelweis, Jenner, Keen, Koch, and Harvey. Perceptive observations were responsible for their achievements).

The healing arts have certainly not reached perfection and "orthodox" medicine has not cornered the market on truth. It is by the alternatives to orthodoxy that medical progress has been made, and a free, progressive society must recognize and protect this right of the physician. (A relevant example is Soviet geneticist T.D. Lysenko who stultified the science of genetics in the U.S.S.R. for a generation by imposing the State sanctioned view that environmentally acquired characteristics of an organism could be transmitted to offspring by inheritance. The Stalinist concept of ideological conformity politically implanted in genetics paralyzed Soviet science in this field).

The treating doctor, the clinician, is at the cutting edge of medical knowledge and a member of that class of persons best qualified to make medical progress. (See Drug Regulation and Innovation—Empirical Evidence and Policy Options, H.G. Grabowsky (1976) which summarizes studies on cost versus benefit analysis of the effects of the 1962 amendment which subjects new drugs to "effective" tests before permitting general prescription and use. Among its findings are: (1) the rate of innovation more than halved by the 1962 amendments with the proportion of ineffective drugs remaining the same, thus, a large decline took place in effective drugs; (2) U.S. drug innovations declined from one-third of worldwide introductions before the 1967 amendment to less than one-sixth of world-

wide introduction afterwards; (3) the 1962 amendment has not enhanced safety because it keeps off the market new drugs that are safer than the drugs they would replace; and (4) one example involving a benzodiazepine hypnotic in use in Great Britain but delayed five years before introduction here could have saved as many as 1200 lives if it had been available in this country. (See also Health Care Reform and Administrative Law: A Structural Approach, Rosenblatt, 88 Yale L.J. 243 (1978) ["The Legal Structure of Health Care Reform: Creating the Appearance of Public Control"].)

The protection of constitutional guarantees of privacy and personal liberty extends not only to the patient pursuing nutritional therapy that includes Laetrile but also to the physician who prescribes and administers the therapy.

C. State interference with cancer victims' constitutionally protected right to obtain and use Laetrile in a program of nutritional therapy is not necessary to further any substantial or compelling State interest.

Those laws are not challenged which prohibit the advertisement of Laetrile as a cure for cancer or which impose standards for labeling, manufacturing, and packaging or which prohibit the sale of Laetrile to members of the general public for the purpose of treating cancer by persons other than licensed physicians. Those regulations serve to strengthen and reinforce the right of

cancer patients to make basic medical decisions which are informed and which can be effectively carried out.

Those laws are challenged which prohibit duly licensed physicians from administering Laetrile to informed consenting cancer patients, and which prohibit the sale of Laetrile to licensed physicians or persons who have obtained prescriptions from licensed physicians. Federal application of Section 505, 21 U.S.C. 355, coupled with the powers of the Commerce Clause has prohibited administration of Laetrile to every cancer victim.

Since these laws directly intrude upon a fundamental constitutional right of cancer victims, they can be given effect to prevent physicians from supplying and administering Laetrile to informed consenting cancer victims only if they are (a) necessary to further a compelling state interest, and (b) they are narrowly drawn to express only the interest of the state at stake. Roe v. Wade, 410 U.S. 113, 155 (1973).

The state has a profound interest in maintaining medical standards and in protecting health and life. This justifies testing and licensing doctors and the limits on giving medical advice by qualified practitioners as well as regulation of pharmaceuticals and licensing of pharmacists and dispensers of drugs. It is also well settled that the state has broad police powers in regulating dangerous drugs in the sense that they are narcotic, habit forming, hallucinatory or toxic. (See Robinson v. California, 370 U.S. 660, 664-65 (1962); and Whipple v. Martinson, 256 U.S. 41, 45 (1921). Their use or misuse "concerns others." Laetrile is not in this

class. It is generally conceded to be a harmless drug. Its alleged evil lies in its "ineffective" treatment of cancer.

The use of Laetrile in the treatment of cancer is not prohibited because Laetrile is harmful or dangerous to the cancer patient or to others. The policy considerations which motivated the prohibition of unapproved substances in general and Laetrile in particular are: (1) A State interest in providing the public with adequate and accurate information with respect to State sanctioned methods for the diagnosis, treatment and cure of cancer; (2) A State interest in protecting cancer patients and their families from deceptive and fraudulent representations regarding the effectiveness of cancer remedies that are not State sanctioned, and (3) A State interest in preventing reliance on methods of treatment which are not State sanctioned and which could, in some cases, delay the use of State sanctioned treatments until such a time as the cancer could no longer be treated or cured by recognized means.

Although the State clearly has a legitimate and substantial interest in promoting these objections, the absolute ban unnecessarily operates to prohibit the use of Laetrile in instances where no legitimate State interest is served.

1. The State Interest In Preventing The Delay Of State Sanctioned Methods of Treatment

Perhaps the strongest State interest advanced in justification of laws prohibiting the use of Laetrile is an inter-

rest in preventing the potential reliance by cancer patients on unapproved treatments to the exclusion of government sanctioned treatments which might be effective in curing or controlling cancer. Thus, the primary evil which these laws envision flowing from the use of Laetrile is the danger that the cancer patient might rely exclusively on Laetrile treatments and that conventional treatments which might cure or control cancer will be delayed until they can no longer be effective.

However, the prohibitions against the use of Laetrile are not narrowly drawn to apply to instances where cancer patients might benefit from conventional treatments. They absolutely prohibit the administration of Laetrile to every cancer victim, including those who are undergoing conventional treatments, those whose conditions are beyond any hope from conventional treatments, those for whom conventional treatments are not indicated, those who have been advised that the dangers of conventional treatments far outweigh any possible benefits, and those who, being fully advised, cannot or will not, subject their bodies to chemicals, radiation or surgery.

The only possible rationale for the absolute ban on the use of Laetrile must necessarily be administrative convenience, for the State interest to be promoted has no application to cancer victims in such individual situations.

However, it is clear that where a law may infringe upon fundamental constitutional rights, the State must narrowly confine the force of the law to the specific objective which justifies

State interference. That is to say, if a particular State objective constitutionally justifies certain State action, the State cannot adopt a law proscribing a broader range of conduct merely to facilitate enforcement or increase the effectiveness of the valid State objective. As this Court said in Stanley v. Illinois, 405 U.S. 645 (1972) at page 656:

The Constitution recognizes higher values than speed and efficiency. Indeed, one might fairly say of the Bill of Rights in general, and the Due Process Clause in particular, that they were designed to protect the fragile values of a vulnerable citizenry from the overbearing concern for efficiency and efficacy that may characterize praiseworthy government officials no less, and perhaps more, than mediocre ones.

It is obvious that the State interest in preventing reliance upon Laetrile to the exclusion of proven treatments could be wholly served by narrowly drawn laws to accomplish that purpose, without an indiscriminate ban that invades the constitutional rights of citizens.

For example, rather than indirectly encouraging treatment by conventional methods, the State could act directly toward that objective by requiring a "monitored" distribution system similar in concept to the monitored system approved by this Court in Whalen v. Roe, 429 U.S. 589 (1977). Any cancer patient who seeks to use Laetrile could register, through their physi-



cian, and provide on a regulation form such information as name and address, diagnosis, type of cancer, history of conventional treatments, progression of the disease, prognosis, and any reasons why the patient seeks to use Laetrile.

Government health officials could review the registration forms and, in the event it appeared that conventional treatments might still be beneficial, could contact the patient and provide the patient with information on conventional treatments.

For those employing conventional treatments concurrently, or whose conditions are hopeless, the State may wish to do nothing. For those declining conventional treatments for religious or personal reasons, the State may or may not wish to do anything.

However, so long as the State cannot veto the ultimate decision of the patient, such a system would be much more likely to serve the State interest, since there would no longer be reasons to seek underground sources of Laetrile or to seek therapy in foreign countries.

Moreover, by permitting a citizen to obtain Laetrile from any physician, it would substantially increase the probability that a cancer patient would be properly diagnosed and advised as to conventional treatments. So long as cancer patients cannot legitimately obtain Laetrile from licensed physicians, thousands are driven to clandestine sources, which have neither the medical expertise nor interest of a licensed physician in fully advising of treatments medically indicated.

## 2. The State Interest In Preventing Fraudulent And Deceptive Practices

It is not disputed that cancer patients particularly those who are beyond benefit from accepted means of treatment, are particularly susceptible to fraudulent representations regarding "miracle" cures. It is also not disputed that the State has a strong interest in preventing the unscrupulous exploitation of desperate victims of this dread disease.

This State interest is reflected in a comprehensive scheme of federal and state laws aimed at prohibiting the defrauding of cancer patients. FDA has ample statutory authority to combat false or fraudulent advertising of ineffectual or unproven drugs (See Food, Drug and Cosmetic Act, misbranded Drugs and Devices, 21 U.S.C. 352 (1976); and Federal Trade Commission Act, Dissemination of False Advertisements, 15 U.S.C. 52 (1975).

Physicians who falsely represent the effect of treatment for cancer face these penalties as well as multiple state statutes for criminal fraud or misrepresentation. The physician who falsely represents the effect of a treatment for cancer is also subject to potentially horrendous civil liability for fraud, assault or negligence. In addition to these penalties, physicians are subject to revocation or suspension of their licenses.

Concerning the licensed physician, this Court in Doe v. Bolton, 410 U.S. 179 (1973) stated at page 199-200:

If a physician is licensed by the

State, he is recognized by the State as capable of exercising clinical judgment. If he fails in this, professional censure and deprivation of his license are available remedies. Required acquiescence by co-practitioners has no rational connection with a patient's needs and unduly infringes on the physician's right to practice. The attending physician will know when a consultation is advisable--the doubtful situation, the need for assurance when the medical decision is a delicate one, and the like. Physicians have followed this routine historically and know its usefulness and benefit for all concerned. It is still true today that '[r]eliance must be placed upon the assurance given by his license, issued by an authority competent to judge in that respect, that he [the physician] possesses the requisite qualifications.'

This does not mean that a physician who misrepresents the effects of Laetrile is immune from criminal prosecution. It is contended, however, that to prosecute a physician who administers Laetrile to cancer victims, at their request, without representing that it will be effective, violates cancer victims' constitutional right to make the ultimate decision with respect to their health.

The absolute ban on Laetrile, however, has nothing to do with the prevention of false or misleading information. It operates to prohibit the use of Laetrile irrespective of what representations are

made by the physician who dispenses it, even if the physician were to advise the patient against its use.

The State interest in preventing fraud is specifically and directly served by a comprehensive range of professional, civil and criminal sanctions which do just that--prohibit fraud and misrepresentations.

Again, at very best it might be argued that an absolute ban serves administrative convenience since if no Laetrile is available, no one will be able to misrepresent its effects. However, such an argument does not even begin to approach the constitutional necessity of limiting the force of a statute to the evil to be remedied without indiscriminately condemning a much broader range of activity not compelled by the specific state interest.

Even if laws directly prohibiting fraudulent and deceptive medical practices were so completely and demonstrably ineffective as to make supplementary regulation necessary, such supplementary regulation could be accomplished by means which are more effective without infringing on the constitutionally protected right of cancer patients to determine a course of treatment.

Thus, rather than an absolute ban on the use of Laetrile or other unapproved substances by physicians the State could, to supplement its fraud laws, institute a mandatory disclosure system enforced by patient registration with the State, under which a physician would be required to provide the patient with materials furnished by the State, or any other information the State feels relevant, and account to the State for having done so.

3. The State Interest In  
Providing Information  
With Respect To State  
Sanctioned Methods Of  
Treatment

The total ban of a particular substance can not inform cancer patients of "approved" methods of therapy. This case illustrates that knowledge of the existence of Laetrile and publicized reports of its benefits to those who have obtained it is widespread. Cancer victims who desire further information must necessarily seek it out of the United States or from an underground source who may or may not be a physician.

A system of mandatory consultation with experts, before Laetrile could be prescribed at the request of a cancer patient, would directly serve rather than tend to defeat the interest of the State.

As this Court held in Planned Parenthood v. Danforth, 428 U.S. 52, 74 (1976), a state may legitimately encourage parental counseling and guidance for minors considering termination of a pregnancy, but it oversteps legitimate state interest where it grants the parent not only the right to consult with the minor but also a veto over her decision. Here the State has vetoed the cancer victim's decision without consultation.

II

The Flat Prohibition Of Laetrile  
Is Not Reasonably Related To The  
Preservation And Protection Of  
The Public Health

In Roe v. Wade, 410 U.S. 113, 150 (1973),

the Court observed that "[T]he State has a legitimate interest in seeing to it that abortion, like any other medical procedure, is performed under circumstances that insure maximum safety for the patient." In Planned Parenthood of Missouri v. Danforth, 428 U.S. 52, 76 (1976), the Court said, "The question ... is whether the flat prohibition of saline amniocentesis is a restriction which 'reasonably relates to the preservation and protection of maternal health.'"

Section 505, 21 U.S.C. 355, as applied, operates to preclude the administration of Laetrile to an informed consenting cancer patient by a licensed physician.

The flat prohibition includes: (1) Cancer victims who have rejected State sanctioned cancer treatments after receiving competent medical advice; (2) Cancer victims who seek to supplement State sanctioned treatments with nutritional treatment that includes Laetrile; (3) Cancer victims who have received competent medical advice that they are too frail for State sanctioned treatments; and (4) Cancer victims who have been diagnosed as terminal by competent medical advisors and informed that State sanctioned treatments have nothing left to offer.

For cancer victims diagnosed as terminal and informed that State sanctioned alternatives are useless, nutritional treatment that includes Laetrile may provide longer, more active lives during their remaining days, and it may be their only hope. For cancer victims too frail for State sanctioned alternatives, nutritional treatment that includes Laetrile is a safer alternative than the more dangerous State sanctioned alternatives.



A law that forces State sanctioned alternatives or nothing at all on these cancer victims is certainly more intrusive than the forcible pumping of a suspect's stomach that the Court found "brutal and ... offensive to human dignity," in Rochin v. California, 342 U.S. 165, 174 (1952).

For cancer victims seeking to supplement State sanctioned alternatives with nutritional treatment that includes Laetrile, and for informed cancer victims who have rejected State sanctioned alternatives, the flat prohibition isolates them from a licensed physician. Cancer victims must seek Laetrile in foreign countries or from underground sources who may care nothing about quality, purity or dosage levels. To be legally deprived of any treatment at all from a licensed physician shows governmental indifference to extreme human suffering. Whatever the intentions of such a law, its effect is surely cruel and inhuman.

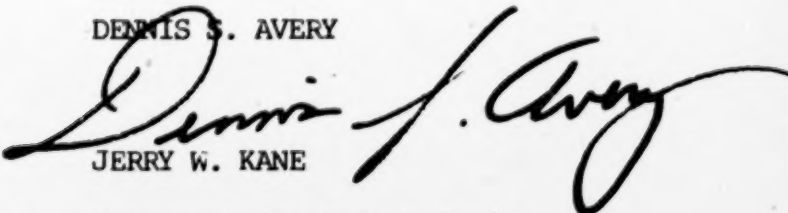
The effect of this law does not insure maximum safety for the patient. In effect, it turns the whole matter of treatment back to the cancer patient himself if he is unwilling to accept the State sanctioned alternatives. Such a law cannot be reasonably related to the preservation and protection of the public health.

CONCLUSION

For the reasons submitted above, amicus curiae, the American Academy of Medical Preventics, respectfully submits that 21 U.S.C. 355, as applied, violates constitutional rights of privacy and personal liberty, and is not reasonably related to the preservation and protection of the public health.

Respectfully submitted,

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IN THE  
**Supreme Court of the United States**

OCTOBER TERM, 1978

No. 78-605

UNITED STATES OF AMERICA, et al.,  
*Petitioners,*

*v.*

GLEN L. RUTHERFORD, et al.,  
*Respondents.*

**Brief Amicus Curiae of The McNaughton Foundation  
of California on Behalf of Robert Stickle,  
Steve Gadler, Dorothy Schires and Mrs. Doris Keith  
Representing a Class of Cancer Patients**

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**INTEREST OF AMICUS CURIAE**

Pursuant to Supreme Court Rule 42(1), this Amicus Curiae brief is submitted on behalf of the class of persons described as American cancer patients who have gone to the Republic of Mexico to receive treatment for cancer including the use of laetrile. These patients number in the thousands. One clinic, Centro Medico Delmar, Tiguana, Mexico, has served in excess

of 15,500 patients since 1974 and currently is receiving patients from the United States at the rate of approximately 3,700 new patients annually. Clinica Cydel, Tijuana, Mexico, has served approximately 3,500 patients since opening its doors and is receiving patients from the United States at the approximate rate of 850 new patients annually.

The staff of these facilities reveal that approximately eighty percent (80%) of the United States patients have come to these clinics after having been advised that their condition is terminal, conventional medicine can give them no further help; they seek treatment with laetrile as a last resort.

Treatment in Mexico by the clinics consists of a special diet, vitamins, minerals and enzymes; adequate rest and exercise; injectable and *oral* laetrile. Radiation therapy, conventional chemotherapy and surgery are used by these clinics at the discretion of the clinic's medical director.

The average stay in Mexico is approximately three weeks. Some patients stay at motels near the border in San Ysidro, California, and travel each day to the clinics approximately ten to fifteen miles away. Some patients stay at motels in Tijuana or in small bungalows provided by the clinics at a moderate rate of \$14.00 per day for double occupancy. After approximately three weeks, the patient's initial course of treatment has been completed and many of the patients have improved to the point where they are ready to continue their treatment at home in the United States. The patient is supplied with a quantity of laetrile, both injectable and oral, as is determined by his attending physician. This initial supply is brought into the United States by the patient upon

presentation of the physician's affidavit and payment of applicable customs duties.

The vast majority of these returning patients desire to continue treatment with laetrile at their homes in the United States. It is at this point that the class of patients in whose interest this brief is being submitted emerges. Under the current affidavit system in use they are permitted to obtain additional supplies upon presentation of the physician's affidavit and the appointment of a properly designated agent for the importation of laetrile. It is this class of patients that will require appropriate relief from this Honorable Court in order to continue their treatment. The vast majority of these patients experience varying degrees of relief and benefits. These patients are generally free from pain without the use of narcotics; the quality of their lives is improved and the length extended.

### SUMMARY OF ARGUMENT

Amicus concurs in the decision of the Tenth Circuit Court of Appeals but requests that this Court should expand the relief granted to the class of patients to include laetrile for oral administration. Whether on the grounds of a determination that the terms "safety" and "effectiveness" have no meaning to the terminally ill cancer patient or on the grounds of right of privacy. Access to laetrile, both intravenous and oral, should not be denied these patients until the clinical trials to be conducted under the direction of the National Cancer Institute, Department of Health, Education and Welfare, have been completed. Amicus urges the continued use of the current affidavit system pending the outcome of these clinical trials.



## QUESTIONS PRESENTED

### I.

WHETHER THE SAFETY AND EFFECTIVENESS REQUIREMENTS OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT SHOULD BE APPLIED TO INJECTABLE LAETRILE INTENDED FOR USE BY TERMINALLY ILL CANCER PATIENTS WHEN PROCURED BY A CERTIFIED LICENSED MEDICAL PRACTITIONER.

### II.

WHETHER THE JUDGMENT OF THE TENTH CIRCUIT COURT OF APPEALS CAN BE UPHOLD BY THE HOLDING OF THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF OKLAHOMA THAT THE DENIAL OF THE USE BY A TERMINALLY ILL CANCER PATIENT OF LAETRILE UNDER THE SUPERVISION OF A PHYSICIAN INVADES THE PATIENT'S RIGHT OF PRIVACY.

## ARGUMENT

### I.

WHETHER THE SAFETY AND EFFECTIVENESS REQUIREMENTS OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT SHOULD BE APPLIED TO INJECTABLE LAETRILE INTENDED FOR USE BY TERMINALLY ILL CANCER PATIENTS WHEN PROCURED BY A CERTIFIED LICENSED MEDICAL PRACTITIONER.

The Federal Food, Drug and Cosmetic Act (Act) defines a new drug as a drug "not generally recognized by qualified experts as safe and effective for its intended use," 21 U.S.C. 321, p. 1.

The decision of the Tenth Circuit Court of Appeals, *Rutherford v. United States*, 582 F.2d 1234, held that "as a matter of law, that the safety and effectiveness requirements of the statute as now written have no application to terminally ill cancer patients who desire to take the drug 'laetrile' intravenously," *ibid.* at page 1237. The Court further limited the procurement of intravenous injections to persons who are certified by a medical practitioner to be terminally ill of cancer.

The Tenth Circuit, in effect, continued the relief granted the patients in the United States District Court on grounds other than that upon which such relief was based in the District Court. Unfortunately, the relief limited the acquisition of laetrile to injectable laetrile.<sup>1/</sup>

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<sup>1/</sup> The term laetrile is being used in this brief to avoid any confusion that might come about by the use of the term amygdalin.

Footnote 1 continued on following page.

It is urged by Amicus that the Tenth Circuit was correct in holding that the Commissioner of Food and Drugs erroneously applied the Federal Food, Drug and Cosmetic Act to the distribution of intravenous laetrile to terminally ill cancer patients. It is strongly suggested that that portion of the decree which permits only intravenous injections of

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Footnote 1 continued

More properly, the subject matter being dealt with before the Court is the substance amygdalin. Amygdalin is extracted from the kernels of various fruits, mostly of the prunus species. Amygdalin is extracted from peach, bitter almond, prune and apricot kernels. The most available is apricot kernels, thus, most of the amygdalin that is extracted is extracted from this source. The term laetrile was first "coined" by Dr. Ernst T. Krebs, Jr. and is now used interchangeably with the term amygdalin. There have been several judicial determinations that have equated laetrile and amygdalin. *United States v. Spectro Foods Corporation*, Civ. - 76-101 (District N.J. 1976) affirmed in part, reversed in part, 544 F.2d 1175 (3rd Cir. 1976); *United States v. General Research Laboratories*, 397 F.Supp. 197 (C.D. Cal. 1975); *Rutherford v. United States*, 399 F.Supp. 1208, 1211 (W.D. Okla. 1979), 424 F.Supp. 105-106 (W.D. Okla. 1977). Cyanogenetic glucosides appear in many foods eaten by man including cassava, sweet potato, yam, maize and millet, bamboo and sugar cane, peas and beans (especially lima beans), kernel of almond, lemon, lime, apple, pear, cherry, apricot, prune, peach and plum, (*Toxic Constituents of Plant Food Stuffs*, C.H. 5, R.D. Montgomery, Academy Press, 1969). (Lest wrong impressions be created by the title of the book "Toxic Constituents of Plant Food Stuffs," it should be noted that upon reading the article by R. D. Montgomery, one would quickly conclude that virtually no danger exists from ingestion of these food stuffs when eaten in normal quantities.)

laetrile should be broadened to include laetrile for administration by oral route.<sup>2/</sup>

(1) The rationale and basis upon which food, drugs and cosmetics are regulated is to protect the unwary customers in vital matters of health. *U.S. v. 250 Jars, etc. of U.S. Fancy Pure Honey*, (D.C. Mich. 1963) 218 F.Supp. 208, affirmed 344 F.2d 288. The line of cases that characterize this as the

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<sup>2/</sup> The current practice by experienced laetrile physicians in Mexico is to commence the treatment of cancer patients with high intravenous doses of laetrile. When the patient's condition justifies it, the patient is switched to a mixture of injectable as well as oral laetrile. This is an integral part of the entire treatment given by these physicians with laetrile. Undoubtedly, the ruling of the Tenth Circuit expressed by inference a possible misunderstanding as to the toxicity of laetrile by oral administration. The same Court also apparently revealed its unfamiliarity with current clinical practice in the administration of laetrile. It should be observed at this point that the route of oral administration presents no danger to the cancer patient when under the guidance of a licensed physician. Laetrile like any other substance, can be ingested in toxic quantities but this is true of many over-the-counter drugs sold without prescription and also of prescription items. This is not a valid reason to withhold it when recommended by a physician. The fears expressed by the U.S. Government and some of the amicus briefs reveal a lack of understanding of the toxicity of laetrile. The American Cancer Society has estimated that as many as 70,000 cancer patients in the United States have received laetrile therapy. This would, by necessity, include oral administration. The report of two deaths which are in themselves suspect and inconclusive leaves much to be desired in supporting claims of the toxicity of laetrile. It is estimated that as many as 1200 deaths occur annually in the United States from ingestion of aspirin. (Center for Disease Control, Atlanta, Georgia.) Yet aspirin is freely available to anyone who wishes to purchase it.

rationale behind the act are numerous, repetitious and center around the attempt to protect the consumer. The requirement of both safety and effectiveness in new drugs as provided by the Act is commendable and should be interpreted and enforced in a rational manner so as to give effect to the underlying purpose. Perhaps it is unworthy to say, but a necessary observation to make, that the safety and effectiveness requirements of the Federal Food, Drug and Cosmetic Act as related to the treatment of cancer is and has been more a statement of wishful thinking than a reality.

Unfortunately, statistics bear out the fact that virtually all methods of treatment of capcerous conditions by accepted modalities are neither "safe" nor "effective."<sup>3/</sup> & <sup>4/</sup>

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(Footnotes 3 and 4 are quoted from Judge Bohanon's decision in *Rutherford v. United States*, 438 F.Supp. 1287.)

<sup>3/</sup> " . . . the treatments that are available are very often disfiguring; they can be painful; they can be unpleasant; they can even be risky." Emil J. Freireich, Professor of Medicine at the University of Texas, School of Medicine, Houston.

<sup>4/</sup> 1977 *Cancer Facts and Figures* by the American Cancer Society estimates that 1977 will have produced an estimated 690,000 new cancer cases; and that over 54 million Americans now living will eventually have cancer, which is one out of every four Americans living. The pamphlet also states that over the years cancer will strike in approximately two of every three families, that in the 1970's there will be an estimated 3.5 million cancer deaths, 6.5 million new cancer cases, and more than 10 million people under medical care for cancer. Only about 1/3 of all people who get cancer this year will be alive five years after treatment, according to the publication.

It is therefore submitted that exceptions to the safety and effectiveness requirements of the Food and Drug Administration have been carved out when dealing with cancer since drugs that are neither safe nor effective have been approved.

Safety is described in the brief by the United States by way of footnote at page 31, footnote 18, "(A) a drug is safe when the expected therapeutic gain justifies the risk entailed in using it . . .", Dr. Theodore G. Klumpp, Chief Drug Division, F.D.A. June 23, 1941.

Therefore, it appears that safety as a term is used in the relative context in relation to the risk involved. Effectiveness relates only to general recognition among "experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs as safe and effective for such use . . .", 21 U.S.C. 321 p. 1.

The foregoing provides little guidance and in the light of the current methods of treatment for cancer, afford little assurance to the cancer patient.

The Tenth Circuit Court of Appeals was able to perceive this within the narrow limitation set forth by that Court. The decision is limited to terminally ill cancer patients and is further limited to intravenous injections of laetrile procured by a licensed practitioner. The Court cited no authority for its decision. Perhaps no such authority exists. However, this Honorable Court has never been bound by authority nor shackled by precedent. In enacting a statutory scheme of regulation such as the Federal Food, Drug and Cosmetic Act, Congress can never be expected to spell out conditions for all



circumstances that may arise in the complex nature of our societies. It is for the judiciary, therefore, to sometimes interpret a statute amidst the realities of life and to base its decision on grounds of reason and principle apart from authority.

The Tenth Circuit Court of Appeals in its decision revealed a depth of understanding of the terminally ill cancer patient's problems. The decision should be upheld but it is again suggested that the Court expand the relief granted to include access to laetrile in the oral administration form.

(2) The brief filed by the United States and that of two amicus briefs (Commonwealth of Massachusetts, State of California) have in greater or lesser degrees claimed inherent dangers from the use of laetrile due to its toxicity and further due to its ineffectiveness. Neither issue is properly before the Court but if unanswered, wrong impressions could be created. Therefore, a few comments should be made relative to these two subject matters.

Initially, it should be observed that as of this date (March, 1979) eighteen states in the United States have legalized the sale, and/or manufacture, of laetrile within those states.<sup>5/</sup>

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<sup>5/</sup> The following states have already legalized laetrile: Arizona, Alaska, Washington, Oregon, Idaho, Nevada, North Dakota, South Dakota, Kansas, Oklahoma, Texas, Louisiana, Florida, Illinois, Indiana, Maryland, New Hampshire, and New Jersey. (Bills have passed in one house of the State Legislature of the states of Michigan and Montana.) It is anticipated with reasonable certainty that a majority of the states will have legalized laetrile within the next year or two.

Amicus will ask the Court to take judicial notice that the legislative bodies of each of the several states have hearings and testimony offered, both pro and con, when considering a bill involving a substance that has apparently been as controversial as laetrile. Amicus will further request the Court to take judicial notice that each of these States, in the exercise of it(s) respective police powers, is primarily concerned with the safety, health and welfare of its citizens. Accordingly, based on this rather overwhelming indication of confidence as expressed by the legislative bodies of the states footnoted below, it becomes apparent that the toxicity claims are appreciably dissipated and the claims of ineffectiveness are similarly suspect. It is not the purpose or the function of this brief to delve into the effectiveness or into the safety of laetrile although on each of these factors, the Court would undoubtedly find some input useful.

The Court should be informed that currently the prestigious Mayo Clinic in Rochester, Minnesota, 55901, is designing a common protocol for the five institutions which have been selected by the National Cancer Institute, Department of Health, Education and Welfare, to carry out the forthcoming clinical trials of laetrile. In a copy of the proposed clinical trial obtained through the Freedom of Information Act, the following statement by Dr. Charles G. Moertel, M.D., of the Mayo Clinic appears as an introductory to the protocol for the clinical trials.<sup>6/</sup>

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<sup>6/</sup> *A Clinical Trial of Laetrile (Amygdalin) in the Treatment of Advanced Cancer*

#### I. Introduction

Laetrile (Amygdalin, Vitamin B-17) is one of the many natural cyanogenic glycosides. This substance was perhaps first isolated by

Footnote 6 continued on following page.

Thus, finally, adequate clinical trials are about to be commenced in which the question of efficacy will soon be

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Footnote 6 continued

German chemists in 1832 and it was listed in the Merck Index in the late 19th century with no defined therapeutic indication.

Current use of Laetrile, dating from the early 1950's, can be ascribed to Dr. Ernest T. Krebs Jr. who theorized 1) Laetrile is metabolized by mammalian cells with the release of cyanide, 2) Detoxification of cyanide by the normal cell occurs promptly, converting free cyanide to thiocyanate, 3) An enzyme inhibition in the cancer cell prevents this detoxification and the free cyanide is therefore allowed to be specifically toxic to the cancer cell.

Animal tumor model studies of Laetrile have been generally stated to show no antineoplastic activity. Initial studies conducted at Memorial-Sloan Kettering by Kanematsu Sugiura, however, were reported as showing delayed appearance and growth of pulmonary metastasis in a spontaneous breast tumor system. He also claimed temporary retardation of growth of small primaries, inhibition of appearance of new tumors, and better health and appearance of treated mice. Later studies at the same institution conducted by Franz Schmidt gave results confirming the observations of Sugiura in one study out of three and this was only at borderline significance. The other two studies were negative. More recent investigations directed by Daniel S. Martin, C. Chester Stock, and Elizabeth Stockert have been uniformly negative. Some of these latter investigations have been blinded and conducted with direct participation by Doctor Sugiura. A large group of animal studies were also conducted at the Southern Research Institute and were stated to be negative, although analyses of these results by some have raised the question of antitumor activity in one of three dosage levels tested. Published negative evaluations in animal model systems also include those of Hill et al (Cancer Res. 36:2102) and Wadinsky (Cancer Chemother Rep 59:939). It must be concluded that in animal tumor studies, the effect of Laetrile has probably been negligible.

Toxicity of Laetrile in dosages currently employed for human cancer is assumed to be minimal, although toxic reactions have never been systematically observed and recorded. Apparently the

Footnote 6 continued on following page.

answered; the question of efficacy belongs in the clinics not in the courts.

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Footnote 6 continued

only observed side effect is transient hypotension immediately following injection, and this is exceedingly rare. Nausea and vomiting have occurred infrequently after oral ingestion and these symptoms are said to subside with continued use. Animal toxicology studies of parenterally administered drug indicate that the dosages currently employed clinically are far below those at which significant toxic reactions would be anticipated. Toxicology of the orally administered drug, however, reveals that there are species to species differences. Though the dose tolerated in dogs is well above that planned in this study the defined Lethal Dose in the monkey and the rat is in the order of 2 grams/m<sup>2</sup>. This is in contrast to the large clinical experience in humans where larger than proposed doses are prescribed and administered with little to no reported toxicity.

In the past, consideration of a clinical trial for Laetrile has been rejected by the medical and scientific community on the basis of inadequate preclinical evidence of antineoplastic activity. The usual criteria for according a new drug high priority for clinical trial, as established by both the National Cancer Institute and the Food and Drug Administration, have included at least a reasonable demonstration of antineoplastic activity in animal tumors. Although complete reliance on rodent tumor experience for admission of drugs to human clinical trial can be scientifically questioned, such a general policy seems reasonable in view of the lack of promising alternative screening procedures for therapeutic activity. A case for waving this precedent could only be made under exceptional circumstances, but such circumstances do now seem to exist for Laetrile. Today in the United States, Laetrile has become one of the most commonly employed chemotherapeutic agents for the treatment of cancer. It has been estimated that during 1977 some 2000 American practitioners were involved in administering over 1,000,000 grams of Laetrile per month to over 50,000 patients. From the standpoint of magnitude of use alone, Laetrile has become a public health issue of major significance.

Footnote 6 continued on following page.

Amicus, representing the class as set forth at the beginning of this brief, would like to briefly touch upon the method by

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Footnote 6 continued

Most important with regard to the Laetrile question are the serious social, economic, political, and legal issues which have surrounded it. Organized medicine, the American Cancer Society, the National Cancer Institute, and the Food and Drug Administration, have previously taken strong stands against the use of Laetrile, but this stance has not seemed to be acceptable to the general public. Organized medicine has been depicted as depriving the dying cancer patient of a harmless treatment that could conceivably provide palliation, and, even if therapeutically inactive, could provide a psychologically beneficial placebo effect. Laetrile has become one of the most popular subject on the news media with heavy coverage in newspapers, magazines, radio, and television. Prominent United States Senators and Congressmen have called publically for a re-evaluation of the Laetrile question and the Senate Subcommittee on Health has held public hearing regarding Laetrile. On the state level, Laetrile has been legalized for either human use or manufacture or both in 17 of the 50 states. Any contention that these actions simply represented a response to a vocal minority would seem to be contradicted by a Harris poll in which a nationwide sampling favored legalization of Laetrile by a strong 53 to 23 percent majority. Laetrile has been, or is being, considered in 16 cases before Federal Courts. In those cases which have been decided, the decisions have overwhelmingly favored Laetrile. Use of Laetrile by the terminal cancer patient has been made legal through Federal District Court decision and this decision has been upheld by the Federal Court of Appeals. This issue is now pending before the United States Supreme Court. Laetrile is now allowed for treatment of any cancer patient, requiring only a short form be filled out which states little more than the patient has cancer and desire such treatment.

Certainly it may be argued that there is a segment of the American public that will pursue quack treatment regardless of what evidence is presented to them. The Laetrile issue, however, has clearly gone far beyond the point of just another quack medicine. Sound, sensible Americans are obviously confused and they are not convinced by the

Footnote 6 continued on following page.

which continued use of laetrile can be experienced by the terminally ill cancer patients pending the outcome of the clinical trials about to be commenced.

Certain references have been made to the "affidavit system." Briefly, this is a system worked out following the orders of the United States District Court for the Western District of Oklahoma following the decision of that Court in *Rutherford v. United States*, 499 F.Supp. 1208. In practice, the system is one in which duly licensed physicians or court approved foreign physicians, may sign affidavits. Cancer patients then, with this affidavit in hand, can obtain their supplies of laetrile as prescribed by their doctor.

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Footnote 6 continued

arguments of Laetrile opponents or by the fact that Laetrile has no activity in experimental animals. Their concern has been overtly expressed by their elected representatives and by their Federal Courts. The welfare of this large segment of the American public cannot be dismissed with the argument that a handful of Laetrile zealots will never be convinced regardless of evidence.

If Laetrile is indeed worthless and a cruel hoax for the cancer victim, then the thinking, sensible American citizen should be presented with convincing evidence that will serve to protect him against such exploitation. If, on the other hand, the widespread public acceptance of Laetrile is indicative of some useful palliative effect, it is even more important that this effect be demonstrated in a convincing manner.

Considering the scope and impact of the Laetrile issue today, there would seem to be no reasonable alternative to a therapeutic trial conducted with objective methodology by experienced clinical cancer research groups whose results will be credible in the eyes of the medical community, the communications media, and the American public.



Amicus strenuously urges the Court that this system (affidavit) should be continued pending the outcome of the clinical tests on laetrile. The thousands of patients that Amicus represents should not be made exiles from their own country in order to continue their treatment. By granting the relief requested, pending completion of the clinical trials of laetrile by the National Cancer Institute, no conceivable harm could be caused to the government's position whereas irreparable harm could be sustained by the thousands of patients Amicus represents should the relief requested be denied and the clinical trials demonstrates the efficacy of laetrile.

## II.

### **WHETHER THE JUDGMENT OF THE TENTH CIRCUIT COURT OF APPEALS CAN BE UPHELD BY THE HOLDING OF THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF OKLAHOMA THAT THE DENIAL OF THE USE BY A TERMINALLY ILL CANCER PATIENT OF LAETRILE UNDER THE SUPERVISION OF A PHYSICIAN INVADES THE PATIENT'S RIGHT OF PRIVACY.**

The government argues in its brief that a terminally ill cancer patient enjoys no constitutional right of privacy which would protect him against an intrusion by the United States Government that would deny him access to the drug laetrile.

Three postulates are urged by the government. The first suggests that (1) laetrile is toxic, the second (2) denies the constitutional right of the patient to take a particular drug or

class of drugs for medical purposes and the third (3) alleges that even if such a constitutional right of privacy exists, such right to use laetrile is outweighed by compelling government interest in protecting the public health. Amicus contends that the United States is wrong on all three postulates.

A. The government first urges that laetrile is toxic. It is interesting to note that the District Court in which nontoxicity was found is the Court in which the evidence was reviewed. Questions of toxicity raised the spectre of possible deaths and the Court was thus entrusted with the sacred task of ruling on a possible death-dealing substance. The U.S. District Court for the Western District of Oklahoma, *Rutherford v. United States*, 438 F.Supp. 1287, found adequate proof by people who had actually used laetrile, as opposed to those who had not, that laetrile indeed was not toxic. The question of toxicity, properly speaking, is not really before this Court. The attempt at this late date to make it an issue before the Court is beyond the scope of this appeal. However, it would be appropriate to repeat that virtually every drug in use today is toxic when ingested or administered by other methods in excessive amounts. When laetrile is prescribed by an attending physician, it is perfectly safe. It should also be noted that a finding by the Commissioner that a drug is not recognized as safe by qualified experts is not a determination of toxicity. The range of safety does not limit itself to toxicity but it involves safety in varying degrees. In any event, when prescribed by a licensed medical practitioner, clearly there is no danger or the spectre of any harm to any person.

B. Next, the government claims that there is no constitutional right of privacy to use unproven or ineffective

drugs. This untenable argument fails to consider the fact that there are no safe drugs or treatments and there are no effective drugs or treatments for the care, treatment or prevention of cancer. Cast in this light, denial of even an unproven or ineffective drug that gives the terminally ill cancer patient hope and is taken by him under the guidance of a physician invades the right of privacy as described by Justice Brandeis in *Olmstead v. United States*, 227 U.S. 438, 478:

"[T]he makers of our Constitution undertook to secure conditions favorable to the pursuit of happiness. They recognized the significance of man's spiritual nature, of his feelings and of his intellect. They knew that only a part of the pain, pleasure and satisfactions of life are to be found in material things. They sought to protect Americans in their beliefs, their thoughts, their emotions and their sensations. They conferred, as against the government, the right to be let alone -- the most comprehensive of rights and the right most valued by civilized men. To protect, that right, every unjustifiable intrusion by the government upon the privacy of the individual, whatever the means employed, must be deemed a violation. . . ."

The cancer patient is left upon the horns of a dilemma; he is offered either unsafe and ineffective remedies sanctioned by the Federal Government or a nontoxic naturally occurring substance which has been present in the diet of man since before the dawn of history. Faced with these alternatives, the terminally ill cancer patient has, and understandably, frequently selected laetrile as his method of treatment. Little has

been said about the improved quality of life that is achieved by the patient receiving laetrile. Appetite is restored, weight increases, pain reduces and the patient experiences an increased sense of well-being. These are the findings of the *California Laetrile Report* of 1953. Within the framework of this circumstance the cancer patients represented by Amicus assert a right of privacy to make this "important decision." To deny him this right is truly an invasion of an area of privacy that has been long recognized by this Court in case after case. This Court has recognized that the right of privacy exists in many areas of our lives. Abortion, *Roe v. Wade*, 410 U.S. 113 (1973), *Doe v. Bolton*, 410 U.S. 179 (1973); marriage, *Loving v. Virginia*, 388 U.S. 1 (1967); procreation, *Skinner v. Oklahoma*, 316 U.S. 535 (1942); contraception, *Eisenstadt v. Baird*, 405 U.S. (1972); family relationships, *Prince v. Massachusetts*, 321 U.S. 158 (1944); child rearing and education, *Pierce v. Society of Sisters*, 268 U.S. 510 (1925). This Court has described the breadth of the right as ". . . independence in making certain kinds of important decisions." *Roe v. Whalen*, 429 U.S. at 599-600. Important decisions are not limited to those areas in which this Court has formerly found this fundamental right to exist.

The Government argues at page 60 of its brief, "the right claimed here of caring for one's health by obtaining a particular drug without government hindrance does not fall into any of those categories." A failure to fall "into any of those categories" (former decisions) does not mean that the right does not exist in other categories. In all probability, it is partly for this reason that this case is before this Court.

This is a case of first impression before this Court. There can be little doubt that this decision, one of life and death, is the type of "important decision" that this Court has recognized in determining the parameters of the right of privacy.

Recently the Supreme Court of the State of California, Sup. Ct. No. CR-32978, \_\_\_ Cal.3d \_\_\_ (1979), had an opportunity to rule on the constitutionality of a State Statute (Health and Safety Code 1707.1) which provides for criminal sanctions to any person, including a physician, who sells, delivers, prescribes or administers any drug or device used in the diagnosis, treatment, alleviation or cure of cancer which has not been approved by the federal agency (21 U.S.C. Section 355) or by the State Board (Cancer Advisory Council) (Health and Safety Code Section 1704).

Defendants, convicted under this statute, claimed a right of privacy in the patient to receive laetrile, the physician defendant claimed a derivative right from his patients. The convictions had been reversed by the District Court of Appeals in California, *People of the State of California v. Privitera, et al.*, 141 Cal.Rptr. 764, in a decision written by Judge Robert O. Staniforth holding that both the doctors' as well as the patients' right of privacy had been invaded. This searching opinion became the opinion of the dissent and was reprinted in the California Supreme Court. The logical arguments of Judge Staniforth are barely resistable. However, the Supreme Court held that the section under scrutiny (1707.1 of the Health and Safety Code of the State of California) did bear a reasonable relationship to the achievement of a legitimate state interest in the health and safety of its citizens.

It should be carefully pointed out, however, that this decision is very narrow in its terms dealing strictly with the constitutionality of the statute in the case under consideration by that Court. A quotation from this case (with apologies for lack of the page number) states as follows:

"Defendants can take no comfort in the Court of Appeals decision for unlike *Rutherford* (referring to 582 Fed. 2d, 1234), this case is not an action on behalf of the class of terminally ill cancer patients. Whatever may be said in favor of permitting terminal cancer patients access to laetrile, there is no indication in the records that defendants sought to restrict their activities to that class when prescribing, distributing and administering laetrile. Indeed, the record reflects that Dr. Privitera sometimes neither took a medical history from, nor personally examined the patients for whom he prescribed laetrile. The lay defendants, of course, were not qualified to diagnose cancer, much less to determine whether a cancerous condition was 'terminal.' " (Emphasis by Court)

Thus it would appear that the California Supreme Court did recognize that terminally ill cancer patients fall within a totally different class; as to them, the right of privacy might easily have been found to exist for this class by the same Court. Certainly this is a reasonable inference.

C. The third argument of the government on the right of privacy contends that application of the safety and efficacy requirement of the Food, Drug and Cosmetic Act to laetrile is a reasonable means of serving a compelling government



interest in protecting the public health. Amicus agrees that the "safe" and "effective" requirements of the Food, Drug and Cosmetic Act are reasonable means of serving a compelling government interest in protecting health. There is no quarrel here. However, this broad statement is not reasonably related to the application of laetrile for reasons previously stated. In *Sands, Statutes and Statutory Construction* (4th ed. 1973), Section 58.04, the following statement appears:

"Because of the deeply entrenched commitment of western society and law to the values of individualism, there is a pervasive preference for interpretations of doubtful statutes which favor individual rights. Thus statutes which impinge on fundamental freedoms are strictly construed." *Dombrowski v. Pfister*, 380 U.S. 479 (1965).

Also, from *Holy Trinity Church v. United States*, 143 U.S. 457 at 459 (1891):

"It is a familiar rule, that a thing may be within the letter of the statute and yet not within the statute, because not within its spirit, nor within the intention of its makers . . . This is not the substitution of the will of the judge for that of the legislator, for frequently words of general meaning are used in a statute, words broad enough to include an act in question, and yet a consideration of the whole legislation, or of the circumstances surrounding its enactment, or of the absurd results which follow from giving such broad meaning to the words, makes it unreasonable to believe that the legislator intended to include the particular act."

It must be remembered that the specific subject matter before this Court is laetrile in its application only to terminally ill cancer patients under the supervision of a licensed physician. The Tenth Circuit Court's decision based upon reason and principle held that "safe and effective" requirements have no meaning to terminally ill cancer patients. Whether the restriction on government regulation of laetrile is thus obtained on a rule of statutory construction or on the constitutional grounds of right of privacy makes little difference to the suffering cancer patient who is told he is about to die. The relief requested is what is needed.

Cancer patients should not be made "exiles" from their own country, they should not be required to go to foreign jurisdictions in order to obtain the laetrile treatment which is a treatment of their own choice.

Finally, it is worthy to comment and speculate that the Tenth Circuit Court sensed the constitutional underpinnings in its decision but indulged in a rule of statutory construction to avoid the constitutional issue which is now before this Court. It is urged that a right of privacy exists in a terminally ill cancer patient to seek and obtain laetrile under the guidance of his physician for his personal use without unwarranted interference by the government.

## CONCLUSION

For the reasons set forth in this brief it is respectfully urged that the Tenth Circuit Court decision should be affirmed, the relief expanded to include oral laetrile. Amicus recommends that the affidavit system now in use should be continued including oral laetrile pending the completion of the clinical trials under the direction of the National Cancer Institute, Department of Health, Education and Welfare.

Respectfully submitted,

STEPHEN TORNAY

*Attorney for Amicus Curiae*

Supreme Court, U. S.  
FILED

APR 5 1979

MICHAEL ROBAK, JR., CLERK

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IN THE  
SUPREME COURT OF THE UNITED STATES  
OCTOBER TERM, 1978

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No. 78-605

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UNITED STATES OF AMERICA, *et al.*,

*Petitioners,*

*v.*

GLEN L. RUTHERFORD, *et al.*,

*Respondents.*

---

ON WRIT OF CERTIORARI TO THE UNITED STATES  
COURT OF APPEALS FOR THE TENTH CIRCUIT

---

BRIEF *AMICUS CURIAE* OF THE "SAVE THE  
UNITED STATES MOVEMENT, IMPROVING  
PUBLIC HEALTH AND PHYSICAL FITNESS OF  
THE UNITED STATES CITIZENS"

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IN THE  
SUPREME COURT OF THE UNITED STATES

OCTOBER TERM, 1978

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No. 78-605

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UNITED STATES OF AMERICA, *et al.*,

*Petitioners,*

*v.*

GLEN L. RUTHERFORD, *et al.*,

*Respondents.*

---

ON WRIT OF CERTIORARI TO THE UNITED STATES  
COURT OF APPEALS FOR THE TENTH CIRCUIT

---

BRIEF *AMICUS CURIAE* OF THE "SAVE THE  
UNITED STATES MOVEMENT, IMPROVING  
PUBLIC HEALTH AND PHYSICAL FITNESS OF  
THE UNITED STATES CITIZENS"

---

OPINIONS BELOW

The opinion of the Court of Appeals (Pet. App. 1a-7a) is reported at 582 F.2d 1234. The opinion of the District Court (Pet. App. 11a-44a) is reported at 438 F.Supp. 1287. The decision of the Commissioner of Food and Drugs (Pet. App. 45a-274a) is reported at 42 Fed. Reg.

39768. The opinion of the District Court rendered after the first hearing, dated Oct. 10, 1975 (hereinafter referred to as the District Court's first opinion), is reported at 399 F. Supp. 1208. The opinion of the Court of Appeals rendered on Oct. 12, 1976, upon appeal from the District Court's first opinion (hereinafter referred to as the Circuit Court's first opinion), is reported at 542 F.2d 1137.

#### INTEREST OF AMICUS CURIAE

The "Save the United States Movement, Improving Public Health and Physical Fitness of the United States Citizens" is an unincorporated, nonprofit organization, founded by Robert Collins Hoffman (popularly known as "Bob Hoffman") of York, Pennsylvania. Mr. Hoffman is the organization's national chairman, its promoter, and its guiding light. Ms. Gertrude Engel of Washington, D.C. is its executive director. The interest of this organization in the present action is predicated entirely on considerations of patriotism, public-spiritedness, and a profound conviction that Americans will be healthier, and stronger if they discipline themselves to follow proper health practices, and if they are freed from unnecessary government intervention in their choice of health regimes. *Amicus* has no commercial interest in Laetrile. All parties to this appeal have filed written consent for the filing of this *amicus curiae* brief.

#### QUESTIONS PRESENTED BY AMICUS

1. Does the Food and Drug Administration's (FDA's) denial of access to Laetrile by banning it from importation and transportation in interstate commerce constitute an unconstitutional invasion of the intended user's (patient's) right of privacy where:

- a) The patient is an informed, adult, consenting, terminal cancer victim;
- b) The patient is acting under the recommendation and care of a licensed physician; and
- c) The Laetrile is to be used solely by the patient, and not otherwise sold or promoted?

2. Is Laetrile entitled to a "grandfather" exemption from the new drug status provisions of section 201(p)(1) of the Food, Drug, and Cosmetic Act, as amended (the Act), 21 U.S.C. 321(p)(1), by virtue of the provisions of section 107(c)(4) of P.L. 87-781?<sup>1</sup>
3. In determining Laetrile's possible "new drug" status, or exemption therefrom, pursuant to the statutory provisions referred to in paragraph 2, above, insofar as that determination may affect the right of an informed, consenting, adult, terminal, cancer patient to have access to such Laetrile for his own consumption, is the FDA, in applying the tests of "safety" and "efficacy" as required by the said statutory provisions, also required to establish reasonable standards adapted to the unusual circumstances of the case, by which the terms "safety" and "efficacy" can be measured?

#### STATEMENT OF THE CASE

This class action (under Rule 23, Federal Rules of Civil Procedure) was initiated by plaintiffs Jimmie Stowe and Gene Sneider, terminally ill cancer victims, on their individual behalf, and that of a class composed of other

<sup>1</sup>This is one of the so-called "transitional provisions" of the 1962 amendment to the Act, reported in the note following 21 U.S.C. 321.

terminally ill cancer victims and their spouses. In anticipation of the demise of both plaintiffs, which demise did in fact occur, the present plaintiff, Glen L. Rutherford, also a terminally ill cancer victim, intervened, and is now identified as plaintiff-respondent in the case now before this Court.

The relief prayed for was an order directing the United States of America, and the Secretary of Health, Education and Welfare to desist from prohibiting the importation and transportation in interstate commerce of that drug known as Laetrile (also referred to as Amygdalin, or vitamin B-17), which order was needed to make possible the preservation of plaintiff's life.

In the first trial of the case on its merits before the United States District Court, W.D., Oklahoma, Judge Bohanon found, on p. 1210, that the plaintiff had been diagnosed, in 1971, as showing an invasive adenocarcinoma, as evidenced by a large prolapsing polyp in the lower colon. Plaintiff's regular physician had strongly recommended an immediate operation, which might involve the removal of plaintiff's rectum. At that stage, plaintiff was considered to be terminally ill. Plaintiff elected to refuse such an operation, and, instead, went to Mexico, where he submitted to a series of Laetrile treatments, administered by a competent physician. As a result thereof, the polyp disappeared completely, without operation, and plaintiff was able to return to his normal work.<sup>2</sup> Plaintiff was advised, however, by his Mexican physician, that he should continue to take Laetrile, as prescribed, in order to prevent a recurrence of his cancer. This he proceeded to do.

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<sup>2</sup> Fortunately, plaintiff is still alive, and well.

In 1975, however, his shipment of Laetrile imported from Mexico, was confiscated by the FDA while still in the hands of the carrier. The latter was jailed, and threatened with a \$10,000 fine. This course of events resulted from the legal processes previously set into motion by the FDA for the purpose of preventing any importation of Laetrile, or trafficking in interstate commerce therein. As a result of said FDA action, plaintiff was deprived of all means of procuring his Laetrile, and felt that he was in danger of dying.

The District Court on October 10, 1975, thereupon granted a preliminary injunction restraining the FDA from prohibiting the further importation of Laetrile destined for the plaintiff, or others in his class.

On appeal to the Tenth Circuit Court of Appeals, (see First Circuit Court opinion) the latter upheld the District Court's temporary injunction, but remanded the case in order that the FDA might hold further hearings, and build a record on the question of Laetrile's new drug status and eligibility for a grandfather exemption.

Such further hearings were, in fact, held by the FDA, which resulted in a reaffirmation of the FDA's original position, and a reissuance of its order prohibiting the importation of Laetrile, and the trafficking therein, in interstate commerce.

Back to the aforesaid District Court for a second trial on the merits, Judge Bohanon again ruled for the plaintiff, and issued a permanent injunction against the FDA forbidding them from interfering with the importation of Laetrile destined for the plaintiff or others in his class, or the trafficking in interstate commerce therein. On the second appeal to the aforesaid Tenth Circuit



Court of Appeals the latter affirmed the decision of the District Court, but on grounds different from those upon which Judge Bohanon had predicated his decision. The case now comes on before the United States Supreme Court, upon a writ of *certiorari*, granted by this Court on January 27, 1979.

### DECISIONS OF THE LOWER COURTS

The District Court found, on p. 1211 of the first District Court opinion, that the plaintiff had been cured of his cancer by the use of Laetrile, that he would have to continue to use it to prevent a recurrence, and that Laetrile was non-lethal, and safe. The Court also found that a new drug application previously had been filed with the FDA on behalf of Laetrile, pursuant to the provisions of section 505(b) of the Act, 21 U.S.C. 355 (b), but that the FDA had not acted on said application either affirmatively, or negatively, within the 180 days allowed by section 505(c) of the Act, 21 U.S.C. 355(c). The Court concluded, therefore, that it (the Court) had jurisdiction to review the matter, since the provisions of section 505(h) of the Act, 21 U.S.C. 355(h) providing for direct appeal to the Circuit Court of Appeals from an adverse FDA ruling on an application for approval of a new drug application were only applicable where the FDA actually took action on the application (either affirmative or negative). Where the FDA merely delayed, through its own inaction, plaintiff was entitled to appeal to the District Court, pursuant to 5 U.S.C. 704 and 706. The Court also concluded that the FDA had the affirmative duty to render a judgment on the new drug application.

On appeal, the Circuit Court of Appeals (in the Circuit Court's first opinion) ruled that the District Court had erroneously held that the FDA was required to make a decision (either affirmative or negative) on a request for approval of a new drug application, if, as was the case here, the application was defective. The FDA has no affirmative duty to conduct such research as would be necessary to correct the defects of the application, and has no duty to act on the application, in the presence of such defects. FDA's responsibility to approve or disapprove the new drug application can only ripen if the application is in proper form. The reason for this is that Congress contemplated that the applicant, and not the FDA, should carry the burden of putting the application into proper form, which entails a long, tedious, and expensive procedure.

However, the Court also held that the determination of whether Laetrile was a new drug, pursuant to section 201(p)(1) of the Act, 21 U.S.C. 321 (p)(1), was to be made by the FDA only as a result of a hearing and a fair and equitable evaluation of the evidence, all of which should be made a matter of record, reviewable by a District Court pursuant to 5 U.S.C. 704 and 706. Such hearing would involve, not only the question whether the drug in question was generally regarded as safe, but whether it qualified for one of the two grandfather exemptions provided by the Act. The case was remanded to give the FDA an opportunity to conduct such hearing.

When the case came before the District Court for the second time, Judge Bohanon decided, first, that Laetrile was not a new drug, by virtue of the grandfather exemption of section 107(c)(4) of P.L. 87-781. Specifically, he found that on the day prior to the enactment of the 1962 amendment to the Act, Laetrile was not a "new

drug," i.e., it was generally recognized among experts qualified by scientific training and experience to evaluate the safety of drugs, as being safe for use under the conditions prescribed. He decided, second, that depriving the plaintiff of the right to obtain Laetrile, under the circumstances of the case, constituted an interference with plaintiff's constitutional right of personal privacy, as guaranteed to him by the First, Fourth, Ninth, and Fourteenth Amendments to the United States Constitution. The injunction against the FDA was thereupon made final.

The Circuit Court of Appeals sustained the results of Judge Bohanon's decision, but predicated its judgment on entirely different grounds. It specifically sidestepped the grandfather and the constitutionality issues. It predicated its decision, rather, on the ground that the tests of "safety" and "efficacy" required by section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1), in determining whether a proposed drug was a "new drug", had no application whatsoever to drugs requested by an informed, consenting, terminally-ill cancer patient, in the absence of special standards by which these terms could rationally be measured. The Court continued the permanent injunction previously issued by the District Court, but limited its application to terminal patients ingesting Laetrile only intravenously, through the ministrations of a licensed physician, and upon his recommendation.

#### EXPLANATORY BACKGROUND MATERIAL ON THE LAETRILE CONTROVERSY

The legal controversy over Laetrile falls outside the mainstream of ordinary litigation. Its precedents are few, and its implications profound. It transcends mere questions of methodology, and furnishes, rather, a forum where two mighty opposing philosophies of medicine

have chosen to join issue. Quite expectedly, the essential facts have become obscured behind a veil of misinformation, not always unwittingly fabricated. The following explanation of the nature of Laetrile and of its relationship to the entire cancer problem serves only to enable the Court better to understand the reasonableness of the Laetrilist position, the nature of the present controversy, and both the subtlety and significance of the latter's dimensions.

Regarding the pervasiveness of the cancer affliction, Judge Bohanon, in ft. 27 of p. 1300 of his opinion, said the following:

*1977 Cancer Facts and Figures* by the American Cancer Society estimates that 1977 will have produced an estimated 690,000 new cancer cases; and that over 54 million Americans now living will eventually have cancer, which is one out of every four Americans living. The pamphlet also states that over the years cancer will strike in approximately two of every three families, that in the 1970's there will be an estimated 3.5 million cancer deaths, 6.5 million new cancer cases, and more than 10 million people under medical care for cancer. Only about 1/3 of all people who get cancer this year will be alive five years after treatment, according to the publication.

Regarding the prominence of the role which Laetrile is currently playing, Charles G. Moertel, M.D. of the Mayo Clinic, Rochester, Minnesota, recently made the following public statement:

Today in the United States Laetrile has become one of the most commonly employed chemotherapeutic agents for the treatment of cancer. It has been estimated that during 1977 over 50,000 cancer patients in America consumed over 1,000,000 grams of Laetrile per month. From the standpoint of magnitude alone, Laetrile has become a public health issue of

major significance . . . . The Laetrile issue . . . has clearly gone far beyond the point of just another quack medicine . . . .

One man who is as well-qualified as any other in the United States to speak authoritatively on the specific subject of cancer research, is the distinguished biochemist Dean Burk, Ph.D., president of the Dean Burk Foundation, who for 35 years was associated as chemist with the National Cancer Institute, National Institutes of Health. As its chief chemist for 16 years, and head of its Cytochemistry Section, he was able to acquire significant insights into the problem of cancer detection and control, which entitle his statements to unusual credibility. His list of publications, memberships, and recognitions is long, and imposing.

For purposes of inclusion in this *amicus curiae* brief, Dr. Burk made the following statement:

Vitamins are organic chemical compounds required by a living organism in calorically negligible amounts for optimal metabolic life functions, and must be supplied in the given organism's diet or nutrition as derived from production by some other organism or by chemical synthesis by man.

Amygdalin<sup>1</sup> is a member of the vitamin B complex (B-17) and thus by definition nontoxic, highly water-soluble, remarkably ubiquitous, and crystallizable. It was first isolated and named in 1830, first

<sup>1</sup>Judge Bohannon, in his decision, in footnote 17 on page 1295, said: "Numerous judicial determinations have been made equating Laetrile and Amygdalin . . . The administrative record clearly establishes that Laetrile and Amygdalin are equivalent, and have been recognized as such for over 20 years."

used to treat cancer in 1843, and first recognized as a vitamin in 1970 by E.T. Krebs, Jr. In animals it has been shown in many laboratories of the world to inhibit cancer growth rates, and cancer spread to other parts of the body (metastases), [and has been instrumental in the] lengthening of life span, or improved health and appearance, as reported extensively in Congressional hearings and scores of scientific articles (any and all statements to the contrary notwithstanding). It has been found to act similarly in a statistically significant fraction of thousands of humans under care of physicians throughout the world, and is currently consumed in the daily diet of upwards of one hundred thousand Americans, as taken either by mouth or injection. Laetrile is consumed by more Americans ill or threatened with cancer than any other single, recognized, chemotherapeutic anticancer agent, with the possible exception of ascorbic acid (vitamin C), . . . . Like all vitamins, vitamins B-17 and C act only under appropriate conditions of their respective dietary deficiencies that give rise to corresponding deficiency diseases, lesions, or symptoms, and their actions may be curtailed or eliminated when other vitamins or food substances are also sufficiently limiting. . . .

Amygdalin has been widely recognized for over one hundred years as nontoxic for man, even at dosages much greater than, in the language of the Act, those which do "not ordinarily render it injurious to health." Conventional dosages taken by untold numbers of Americans range from one to twenty grams daily, without notable toxicity or pharmacologic injury. . . . For over one hundred years standard pharmacology and toxicology compendia have indicated that amygdalin is nontoxic by standards accepted as nontoxic. . . .



The relevant literature discloses an unbridgeable gap between the basic thinking of Laetrilists and anti-Laetrilists. The high tension generated by the resultant controversy is explainable, not alone by the fact that countless cancer victims consider their right to Laetrile a matter of life or death, literally, but that those tens of thousands of professional reputations, and staggering investments of time and money presently committed to establishing the anti-Laetrilist point of view would be, if that point of view were successfully challenged, seriously undermined, and the comfortable respectability of current medical practices reduced to shambles.

The logic behind current medical opposition to Laetrile was explained by Ms. Gertrude Engel, executive director of the organization in whose behalf this *amicus curiae* brief is filed, and who has had many year's experience in the promotion of sound nutrition and related sound health practices. In a recent statement, Ms. Engel, who is also a columnist, said:

The opposition of medical orthodoxy to Laetrile is at least understandable, if not justifiable. Because doctors, generally, have had no experience with Laetrile, they fear it. It is new. It is different. It seems like an absurd oversimplification. If apricot pits can do more against cancer than five billion dollars worth of radiation equipment, and the whole frightening panoply of anti-cancer weapons, then where do the doctors and technicians, the medical colleges and professors, and the learned medical journals go from here? Moreover, there is always the specter of malpractice suits. As long as a physician follows the well-beaten path of consensus therapy, he knows he is solidly safe against the assaults of irrationally-emotional cancer victims. But once,

when the going is tough, the support of his colleagues is withdrawn, what kind of legal pitfalls lie ahead? The risks are frightening, which only the most robust of practitioners are willing to take.

Dr. Ernest T. Krebs, Jr., biochemist in San Francisco (who is considered the father of Laetrile), propounded the theory, in 1952, that:

cancer, like scurvy, and pellagra, is not caused by some kind of mysterious bacterium, virus, or toxin, but is merely a deficiency disease aggravated by the lack of an essential food compound in modern man's diet. He identified this compound as part of the nitriloxide family which occurs abundantly in nature in over twelve hundred edible plants. . . . It is particularly prevalent in the seeds of those fruits in the *prunus rosacea* family (bitter almond, apricot, blackthorn, cherry, nectarine, peach, and plum), but also is contained in grasses, maize, sorghum, millet, cassava, linseed, apple seeds and many other foods that, generally, have been deleted from the menus of modern civilization.<sup>3</sup>

Informed Laetrilists, who generally accept the above thesis of Dr. Krebs, approach the cancer problem, not with the objective of trying to find some miracle treatment that can destroy, by excising, burning, or poisoning the visible manifestations of cancer (polyps, tumors, lesions, etc.), but to find and remove the *underlying causes*, or *conditions*, of cancer, which, according to them, are associated with a metabolic deficiency.

Laetrilists fault medical orthodoxy for failing to distinguish between:

- a) Cancer symptoms;

<sup>3</sup>Quoted from: "World Without Cancer", by G. Edward Griffin (1977 reprinting), pp. 51, 52.

- b) Immediate causes of cancer, or "triggering agencies" such as tobacco smoke or carcinogen-impregnated air, or unnatural stresses, and physical or chemical irritants; and,
- c) The underlying cause, or condition, of cancer, which is a metabolic deficiency.

If the underlying cause is identified and removed, it is reasoned, the symptoms and triggering mechanisms become of secondary importance. Moreover, from a pragmatic point of view, it makes more sense to concern ourselves with the basic cause or condition of cancer, since, according to Laetrilist orthodoxy, that cause is associated with a single, relatively easily-understood concept, whereas the mechanisms which trigger off the manifestations or symptoms of cancer are almost infinite in number, and, by very definition, can never be completely understood, or, *a fortiori*, removed.

The Laetrile erudites generally consider cancer cells to be similar, if not identical, to trophoblast cells which, during pregnancy, manufacture the tissues forming the umbilical cord and placenta, but which, after their task is done, cease all further proliferation because of the action of certain growth-arresting enzymes which the body manufactures for that purpose. When, due to a nutritional deficiency or other causes, this natural defense does not function adequately, the body becomes vulnerable to the uncontrolled proliferation of cancer cells.

The remedy, according to Laetrilists, is to restore the patient's proper natural metabolic balance through administering large doses of that deficient nutritional element needed to enable the body to combat the cancer. This approach is reminiscent of the epoch when scurvy

was first found to result from a vitamin C deficiency. The remedy: heavier doses of vitamin C.

The above explanation, of course, is an oversimplification of both the problem and the solution. The complications are many. One of them is the fact that after cancer cells have extensively proliferated into vital areas of the body, and after the patient has subjected himself to injurious surgery, radiation, and/or chemotherapy, the probabilities are that serious damage will have been caused to vital organs, and to the body's natural defense mechanism. Even the most effective cancer remedy cannot render whole an organ which has been irreparably damaged either by cancer, or by destructive cancer treatments.

The Laetrilists take the position that too many resources (which total millions of hours in time, and billions of dollars in wealth) have been spent in a futile search for ways of reducing cancer symptoms, and not enough in finding out what cancer really is. As a result, the bottom-line statistic on cancer recovery, after treatment, is appallingly bad, and has scarcely improved in a hundred years.

As stated by John A. Richardson, M.D., who has had long experience with the administration of Laetrile (but who, incidentally, was barred from practicing medicine in California for that reason):

No longer were we treating the lump or bump; we were treating the entire patient. While the medical profession continued to think of cancer as a *tumor*, we recognized it as a systemic *condition*. A lump, or bump is merely the symptom, not the disease itself. No wonder we doctors had failed to control cancer

all these years. We had been attacking the symptom and ignoring the disease.<sup>4</sup>

Glen D. Kittler, summarized the difference between the two approaches in the following words:

Scientifically, there has always been a canyon between the Laetrilists and the anti-Laetrilists. The anti-Laetrilists, sometimes called the Cancer Establishment, have maintained that cancer is a multiplicity of diseases—perhaps hundreds—which all exhibit themselves in one way—cancer. The Laetrilists, on the other hand, have maintained that cancer is a single disease with a multiplicity of exhibitions. From the point of view of the Establishment, then, it would seem highly unlikely that medical science will ever overcome cancer. The Laetrilists, however, at least provide a starting point and a direction to go.<sup>5</sup>

The following general propositions regarding Laetrile must be made at this juncture:

1. Informed Laetrilists do not all agree on the precise rationale to explain the effectiveness of Laetrile therapy. They are in total agreement, however, that we stand only on the threshold of understanding the vital forces at work in making Laetrile effective. Much work yet needs to be done to unlock the mysteries of this promising cancer treatment.
2. Laetrilists are modest in their claims for Laetrile's effectiveness. They are unanimous, however, in their insistence that the percentage of

<sup>4</sup>"Laetrile Case Histories", p. 11 by John A. Richardson, M.D. and Patricia Griffin, R.N. (1977 edition).

<sup>5</sup>"Laetrile, Nutritional Control for Cancer with Vitamin B-17", by Glenn D. Kittler, revised edition, 1978, page 9.

Laetrile patients whose cancer has been "controlled" (as opposed to "cured") is significantly higher than that of patients treated with orthodox remedies, under comparable conditions.

3. Laetrilists point out, however, that entirely apart from the percentage of cancer patients whose cancer has become "controlled" through the effects of Laetrile, there are literally hundreds of thousands who have received other types of very tangible benefits, such as relief from pain and distress and loss of weight. More important, they have been spared the brutal, humiliating, and degrading therapy which is sometimes required by traditional methods, involving the loss of genitals, breasts, rectum, etc. Measured by these immediate benefits, alone, it is argued, Laetrile has justified itself.
4. Laetrilists agree with anti-Laetrilists that early diagnosis and treatment of cancer is requisite for maximizing the chances of recovery. Delay in receiving treatment may result in destruction of whatever opportunity there is for controlling the cancer (although the cancer patients whose illness had been declared "terminal" by orthodox medicine, and whose cancer has subsequently been brought completely under control through the use of Laetrile, number in the many thousands.)
5. Laetrilists agree that Laetrile should be administered only to cancer patients, (but certainly should not be limited to terminal patients) upon recommendation, and under the care, of a competent physician, after giving informed consent. *Under no circumstances* should Laetrile become an over-the-counter drug.



6. As more light is shed on the subject, the view of most Laetrilists will be confirmed that Laetrile will only be minimally effective unless administered in connection with:

- a) A strict dietary regime which stresses the importance of foods which do not place an unnecessary digestive load on the pancreas;
- b) The ingestion of extra vitamins (in addition to B-17), and enzymes.

It follows that the beneficial results of Laetrile will depend in large measure on the intelligence of the patient, and his or her willingness to follow rigid dietary strictures.

Admitting as they do that there is still much to learn about Laetrile and its supporting rationale, Laetrilists contend that in view of the fact that:

- a) Laetrile has been endorsed by many of the world's most informed men in the field of cancer (as will be pointed out further in this brief);
- b) Research in the area of Laetrile therapy has shown it to be more fruitful of results than conventional therapy, both in controlling cancer, and in bringing relief from pain and avoiding the necessity of enduring expensive, excruciating, and degrading conventional treatments;
- c) Laetrile stands up well against the government-sanctioned alternatives; and
- d) Laetrile has reached and passed the threshold of rationality as an alternative to orthodox therapy;

the law should not make criminal that commerce in Laetrile destined for those who desire it for their own use. The lowly apricot pit, and its derivatives and cog-

nates, may turn out to be the most generous medical benefactor yet discovered by man.

This background discussion on Laetrile is concluded with a quotation of Stewart M. Jones, M.D. and Ph. D. (Palo Alto, California), an authority in this field, as follows:

This theory [of Laetrile] is the oldest, strongest, and most plausible theory of cancer now extant. It has stood the test of seventy years of confrontation with new information about cancer without ever being disproved by any new facts. . . . The voluminous heterogeneous science of cancer developed since then is coherent only in the light of this theory.<sup>6</sup>

#### SUMMARY OF ARGUMENT

In this brief it is assumed, without conceding, that Laetrile is a drug, as well as a food, under the provisions of section 201(g)(1)(B) of the Act, 21 U.S.C. 321 (g)(1) (B), for the reason that within the mind of the general consuming public Laetrile has become associated with an intended use in the diagnosis, cure, mitigation, treatment, or prevention of cancer. It is assumed that plaintiff, and those in whose behalf this action is brought, are informed, consenting, adult, terminal, cancer victims, who have elected to submit themselves to Laetrile treatment, upon a competent physician's recommendation, and under his supervision. It is *not* assumed that the treatment involved is limited to intravenous injection. *Amicus's* first argument is that, under these circumstances, the making criminal of, or interdiction, or interference in any way by the United States Government, or

<sup>6</sup>"Nutritional Rudiments in Cancer," Stewart M. Jones, M.D., p. 6.

any of its agencies with, the importation or the transportation in interstate commerce of Laetrile destined for the intended user's (patient's) sole use, and not for sale to another or for general promotion, constitutes an unconstitutional invasion of the patient's right of personal privacy guaranteed to him by the provisions of the First, Fourth, Fifth, and Ninth Amendments to the United States Constitution.

This is for the reason that the invasion of one's individual right of privacy, which includes the freedom to choose the health regime applicable to one's own body, must not be violated except in the presence of an overriding substantial and compelling State interest. The alleged overriding substantial and compelling State interest in support of FDA's strictures placed upon the trafficking in Laetrile, namely that of discouraging cancer patients from resorting to unproven cancer remedies which might discourage, to their detriment, their timely recourse to state-sanctioned alternatives, is not of sufficient weight to override the patient's right of privacy.

Some of the factors which the Court is entitled to consider in balancing the State's interest in protecting its citizens from inflicting self-injury, against the citizens' right to select their own medical therapy, are the following.

1. Whether the therapy is safe;
2. Whether the therapy is reasonable, and relatively effective vis-a-vis its state-sanctioned alternatives. "Effective" includes not only controlling or curing the disease (cancer), but realizing other benefits, such as: relieving pain, increasing the quality of life, and eliminating the need for other excruciating, and

destructive state-sanctioned remedies which frequently do more harm than good;

3. Whether the patient is an informed, consenting, adult, terminal, cancer patient, receiving his Laetrile on doctor's advice, and under his supervision;
4. Whether there is a rational connection between the alleged paramount State purpose (to discourage a self-destructive recourse to non state-approved alternative remedies) and the means employed to accomplish that purpose (the making criminal and interdiction of trafficking in Laetrile).

It is not argued that all of the above factors must be resolved in favor of the plaintiff in order to support the paramountcy of the right of individual privacy over the State's right to prevent self-inflicted injury (i.e., to proscribe traffic in Laetrile). A favorable resolution of item number one, above, would probably be sufficient in itself. A combination of numbers one and three should be sufficient, without question. A favorable resolution of the other two items makes the case that much stronger.

Since all the above factors can be favorably resolved, in the instant case, in favor of the plaintiff (Laetrile), the case is much stronger than would be minimally necessary to justify a judgment sustaining the position of the federal District Court.

*Amicus's* second argument is that Laetrile is not a new drug, for the reason (among others) that it is exempt by virtue of the provisions of section 107 of P.L. 87-871, appearing in the note following 21 U.S.C. 321. This is one of the two grounds upon which District Court Judge Bohanon predicated his second opinion.

*Amicus's* third argument is that when applicable to an informed, consenting, adult terminal cancer patient, the tests of "safety" and "effectiveness" as required by section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1), have no meaning in the absence of special standards applicable to those circumstances.

In the absence of such standards, the tests cannot be rationally applied, and Laetrile cannot be considered a new drug, and its importation proscribed, insofar as the proscription would deprive plaintiff of his Laetrile. *Amicus* contends that terminal cancer patients are as entitled to "safe" drugs as any other patient, but that rational standards are required, before the test can be applied. However in view of the fact that the District Court found from the record that Laetrile was generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as being safe, and thus meeting the requirements of section 201(p)(1) of the Act, 21 U.S.C. 321(p)(1), the consideration of this point, insofar as it relates to safety, is moot.

## ARGUMENT

### I.

**THE MAKING CRIMINAL, OR ENJOINING (1) THE IMPORTATION OF A NEW DRUG, OR (2) THE INTRODUCTION OF A NEW DRUG INTO INTERSTATE COMMERCE, BY THE UNITED STATES GOVERNMENT, CONSTITUTES AN INVASION OF THE INDIVIDUAL RIGHT OF PRIVACY GUARANTEED TO THE INTENDED USER (PATIENT) BY THE FIRST, FOURTH, FIFTH, OR NINTH AMENDMENTS TO THE CONSTITUTION OF THE UNITED STATES, WHERE THERE ARE NO OVERRIDING SUBSTANTIAL AND COMPELLING STATE INTERESTS REQUIRING IT. WITH REGARD TO THE NEW DRUG LAETRILE, UNDER THE CIRCUMSTANCES OF THE PRESENT CASE, THERE ARE NO SUBSTANTIAL AND COMPELLING STATE INTERESTS OVERRIDING THE PATIENT'S INDIVIDUAL RIGHT OF PRIVACY.**

This honorable Court can, with propriety, address itself to the constitutional aspects of the case before it, because of the Constitution's uncertain application to the facts of this case, and the great numbers of persons upon whom the determination of such constitutional issues will have heavy impact. On page 9 of this brief was set forth an estimate of the number of persons now using Laetrile and to whom its continued use constitutes literally a matter of life or death.

In the present case, what is basically involved is the right of a terminal cancer patient, acting under the direction of his physician, and being fully advised in the premises, to make his own choice of treatment for his fatal disease, in the desperate hope that the treatment of his choice (in this case Laetrile) might succeed in reducing the hideous probabilities that his disease will prove fatal, or if it does not so succeed, then that it might at least bring him a surcease from his physical



suffering. This right of choice in matters involving the health and care of one's own body is a very important application of the broad right of "privacy" which is becoming increasingly dear to human beings who find themselves living in a world of increasingly diminished privacy.

In the case of *People v. Privitera*, 141 California Reporter 764 (1978), which involved a criminal action against a doctor whose administering of Laetrile to his cancer patients was deemed in violation of the California Statue forbidding non-approved cancer remedies, the court said, on page 786:

Historically this right of privacy was first articulated as constitutional right in *Griswold v. Connecticut*, 381 U.S. 497, 85 S. Ct. 1678, 14 L. Ed.2d 510, a decision holding unconstitutional a statute prohibiting the use of contraceptives. However, the recognition of the existence, innate in every human being, of a zone of privacy is older than the Bill of Rights, older than our political parties, older than the state's concern with the nature of treatment to be received by cancer-ridden patients. It is in the nature of man that such right exists.

This principle, now of constitutional dimension, has been embraced by many decisions in a variety of situation. (See *In re Lifschutz*, 2 Cal. 3d 415, 432, fn. 12, 85 Cal. Rptr. 829, 467, P. 2d 577 and *Roe v. Wade*, 410 U.S. 113, 151-153, 93 S.Ct. 705, 726, 35 L. Ed. 2d 147). This concept, when placed in the doctor-patient relationship is the "right to decide independently, with the advice of his physician, to acquire and to use needed medication." (*Whalen v. Roe*, 429 U.S. 589, 97 S.Ct. 869, 876, 878, 51 L. Ed. 2d 64; *Doe v. Bolton*, 410 U.S. 179, 197, 93 S.Ct., 739, 750, 35 L. Ed. 2d 201.)

*In re Lifschutz*, supra 2 Cal.3d 415, 431, 432, 85 Cal. Rptr. 829, 840, 467, P. 2d 557, 568, makes this profound insight concerning *Griswold*:

Indeed, the decision's concern for valued aspects of individual privacy may ultimately aid in protecting man from the dehumanization of an ever-encroaching technological environment.

The fundamental nature of the right of privacy derives from the very nature of man himself. This thought was clearly expressed by Justice Brandeis in *Olmstead v. United States*, 277 U.S. 438, 478, 48 S.Ct. 564, 572, 72 L.Ed. 944 in the following language:

The makers of our Constitution undertook to secure conditions favorable to the pursuit of happiness. They recognized the significance of man's spiritual nature, of his feelings and of his intellect. They knew that only a part of the pain, pleasure and satisfactions of life are to be found in material things. They sought to protect Americans in their beliefs, their thoughts, their emotions and their sensations. They conferred, as against the government, the right to be let alone-----the most comprehensive of rights and the right most valued by civilized men. To protect that right, every unjustifiable intrusion by the government upon the privacy of the individual, whatever the means employed, must be deemed a violation. . . .

Judge Cardozo in *Schloendorff v. Society of New York Hospital*, 211 N.Y. 125, 105 N.E. 92, at 93, stated:

Every human being of adult years and sound mind has a right to determine what shall be done with his own body.

There is no question but what, as a general rule, the state has the right to regulate the delivery of health

services, *Barsky v. Board of Regents of University*, 347 U.S. 442, 449, 74 S.Ct. 650, 654, 98 L.Ed. 829; *People v. Nunn*, 46 Cal.2d 460, 469, 296 P.2d 813. It is generally conceded that doctors may be prohibited from administering certain types of harmful or habit-forming drugs, under certain circumstances, *Blinder v. Division of Narcotic Enforcement*, 25 Cal. App. 3d 174, 101 Cal. Rptr. 635. To put it simply, the Courts recognize the State's interest, pursuant to its legitimate exercise of police power, to discourage or restrain self-injury or suicide. However, in the exercise of this power the means used must be reasonably necessary for the accomplishment of that public purpose, *Goldblatt v. Town of Hempstead, New York*, 369 U.S. 590, 594, 595, 82 S.Ct. 987, 990, L.Ed.2d 130.

Judge Bohanon, in his opinion, said at p. 1295:

While the Constitution does not explicitly mention a right of personal privacy, it is unchallengeable "that a right of personal privacy, or a guarantee of certain areas or zones of privacy, does exist under the Constitution." *Roe v. Wade*, 410 U.S. 113, 152, 93 S. Ct. 705, 726, 35 L.Ed. 2d 147 (1973). This right has been discerned within the penumbras of the Bill of Rights, and specifically within the language of the First, Fourth, Fifth, Ninth, and Fourteenth Amendments to the Constitution, *Roe v. Wade, supra*, "... only personal rights that can be deemed 'fundamental' or 'implicit' in the concept of ordered liberty,' ... are included in this guarantee of personal privacy."

Mr. Justice Douglas referred to "the freedom to care for one's health and person" as coming within the purview of this right. *Doe v. Bolton*, 410 U.S. 179, 213 (1973), 93 S.Ct. 789, 758, 35 L.Ed.2d 201 (concurring opinion). "The right of privacy,"

Justice Douglas proceeded, "has no more conspicuous place than in the physician-patient relationship. . . ." *Doe, supra* at 219, 93 S.Ct. at 761. He concluded: "The right to seek advice on one's health and the right to place reliance on the physician of one's choice are basic. . . ." *Doe, supra*.

#### A. Laetrile is Safe, and Not Dangerous to Human Health

This brief does not question the right and duty of the FDA to promulgate reasonable regulations proscribing trafficking in drugs which are considered unsafe or dangerous to human health when taken under the conditions prescribed, recommended, or suggested in the labeling thereof. However, the safety, or non-toxicity of Laetrile cannot be reasonably called into question. Judge Bohanon, when this case was first before him, found, at page 1212:

The Court finds from the record, testimony and exhibits, that laetrile is not lethal in any sense of the word. It is not harmful to the human body and when used in proper amounts under proper control and supervision can effect relief from cancer disease to the satisfaction of many who are privileged to use the same.

The Court in *People v. Privitera, supra*, found, on page 778, that:

"It [Laetrile] is generally conceded to be a harmless drug."

and again, on page 767:

"It is generally conceded that amygdalin is non-toxic; it does not fall within the general ban of drugs which are toxic, habit forming, addictive, or otherwise distort reality."

Judge Bohanon, in his second decision in the instant case found, on page 1295:

The record and the law reasonably support but one conclusion: Laetrile (Amygdalin) has been commercially used and sold in the United States for the treatment of cancer for well in excess of 25 years, during which time it has been "generally recognized" by qualified experts as safe for such use.

. . . [page 1297] The administrative record brooks little real controversy as to Laetrile's nontoxicity, particularly when administered parenterally, even at doses greatly exceeding amounts normally ingested.

<sup>23</sup> In the only laboratory study of record specifically designed to determine the drug's toxicity, it was observed: "Amygdalin, at all doses studied, appears to be completely non-toxic in laboratory mice." Harold W. Manner, Ph.D., Chairman, Department of Biology, Loyola University, Chicago, Illinois (R 262). Of the various controversial tests studying Laetrile's efficacy on animal tumors, none have disclosed toxicity at reasonable dosage levels.

Among the numerous scientists and physicians testifying from first-hand experience with Laetrile and its effect on humans, unanimity exists as to its nontoxicity.

Dr. Phillip Binzel, M.D., graduate of St. Louis University, testified that he has personally given nearly 4,000 intravenous injections of Amygdalin using doses up to 9 grams without any adverse reaction. (tr. 363).

Daniel S. Martin, M.D., who participated in the same Sloan-Kettering experiments in which Dr. Sugiura detected cancer inhibiting properties in Laetrile, and who disputed Dr. Sugiura's results,

nonetheless concluded that there was no doubt that Laetrile was nontoxic, at least if administered parenterally. (Tr. 437).

Charles Gurchot, Ph.D., testified for the record in affidavit form that Amygdalin in liquid and solid form was used prior to 1962 (between 1934 and 1945) by Gurchot, under supervision of five named medical doctors at the University of California Medical School at San Francisco. This Amygdalin was, according to his statement, administered "on patients intramuscularly and intravenously." He further stated that during this same period Amygdalin was being used to his personal knowledge by approximately a dozen California physicians in their treatment of cancer. Gurchot expresses his belief that Amygdalin was generally recognized by experts as being safe for use in the treatment of cancer on or prior to October 10, 1962. (R 302 at J-206).

Chauncey D. Leake, Ph.D., indicated in his affidavit that he is familiar with Dr. Gurchot's use of Amygdalin in the mid 1930's and 1940's at the University of California Medical School Hospital in San Francisco. He further indicates that physicians and other scientists familiar with Amygdalin recognized it as safe at that time. (R 302 at J-200).

Dr. Dean Burk, former head of the Cytochemistry Section, National Cancer Institute, Bethesda, Maryland, after testing Amygdalin on rats, says the substance is "notably less toxic to animal organisms than ordinary diet sugar," and that aspirin tablets are 20 times more toxic than an equivalent amount of Amygdalin (R 183 at 166F).

Investigators have found that intravenous doses in excess of 20 grams have been without toxic effect in healthy human subjects, although occas-



sionally a mild hypotensive effect may be observed. Repeatedly, studies have indicated that pure Amygdalin, when administered parenterally is astonishingly devoid of toxic effects. (R 163 at 166F).

Donald C. Thompson, M.D., of Morristown, Tennessee, testified as to his personal experience with administering Laetrile to patients and affirmed the drug's nontoxicity. (R 515).

In his report entitled "Use of Laetrile in the Prevention and Treatment of Cancer," Dr. David Rubin, M.D., surgeon at Beilinson Hospital and cancer researcher at Hadassah Hospital in Jerusalem, Israel, asserts: "Laetrile is nontoxic even in very large injected doses." (R 510, Ex. 12).

As another example of a practicing physician who has extensively used Amygdalin and determined it to be nontoxic, see the letter of The Honorable Lawrence P. McDonald, Congressional Representative from Georgia. (R509 at N265-68).

'Amygdalin (Laetrile) is totally non-toxic systemically, at commonly applied dosages.' Hans A. Nieper, M.D., Hannover [sic], West Germany. (R 302 at J-180).

While a doctor's inability to control many variables potentially relevant to curing a disease may impugn the credibility of his perceptions as to a drug's efficacy (see *Weinberger v. Hynson, supra*) his observations as to its toxicity are much more reliable, since the relevant variables are more manageable.

"[Laetrile] is totally nontoxic. Its lethal dose in mice and rats, by injection, is about 25,000 milligrams per kilogram of body weight. It is so nearly nontoxic that in some studies the water,

used as a dilutant presents a greater toxicity than the vitamin." *The Journal of Applied Nutrition*, Ernst T. Krebs, Jr. (R 302 at J-187).

"... All the available facts indicate that Amygdalin is essentially non-toxic to laboratory animals and to humans." Raymond Ewell, Ph.D. in chemistry from Princeton, retired professor from the State University of New York, at Buffalo. (R 302 at J-196).

Dr. John A. Richardson, previously referred to, in his book "Laetrile case histories" (1977), says, on page 23:

One of the reasons given for refusing is that Laetrile might be toxic. They [the F.D.A.] said:

'It is dangerous to initiate human studies while the nature of the toxicity has not been elucidated in large animal species.'

To anyone with any knowledge of the subject at all, that is an incredible statement. Amygdalin has been well known and listed in the *United States Pharmacopeia* as a non-toxic substance for over a hundred years. The human case studies submitted by McNaughton were further proof of its safety. To deny permission to test on the grounds that amygdalin may be toxic is mind-boggling when one realizes that virtually all drugs currently approved by the F.D.A. for cancer therapy are *extremely toxic*.

**B. Laetrile is a Reasonable and Relatively Effective Cancer Remedy, vis-a-vis its State-Sanctioned Alternatives. "Effective," in this Context, has Reference, not only to Controlling or Curing Cancer, but Providing other Substantial Benefits to the Patient, such as Decreased Pain, Improved Quality of Life, and Avoidance of Excruciating, and Expensive, State-Sanctioned Alternative Remedies.**

This Court is not called on, of course, to place a final evaluation on the claims on behalf of Laetrile, vis-a-vis its state-sanctioned alternatives. It is entitled, however, to satisfy itself, from the evidence contained in the record, that there is enough testimony in favor of Laetrile to indicate that it has at least crossed a sufficiently acceptable threshold of rationality to indicate that the patient's preference for it is neither suicidal nor irrational.

We have, here, a clear collision between two conflicting doctrines: the one declaring that the state has a legitimate interest in preventing people from seriously injuring or killing themselves, and the other declaring that people should be free to choose their own form of therapy. Where to draw the line between those two doctrines is what this case is all about.

The FDA faces a particular difficulty in relating its proscriptions of Laetrile to the first doctrine above mentioned (protecting people from self-injury). The reason for this is that the respective risks and benefits of the State-sanctioned remedies (surgery, radiation and/or chemotherapy), and those of the State non-sanctioned remedy (Laetrile) are almost impossible to compare by

any objective and generally-agreed-upon standard of comparison. If State-sanctioned remedies were to lead to complete, or virtually complete, recovery from cancer, and if Laetrile were to lead to certain, or virtually certain death or risk of death, the legal issue would be clear-cut and simple. The actual facts are, however, that the results of the State-sanctioned remedies, viewed in their most favorable light, are woefully disappointing (only one out of three cancer patients currently alive will still be alive in five years), and the results of Laetrile are sharply controverted, the government arguing that the Laetrile patient's chances of recovery are considerably less than those associated with State-sanctioned remedies (or even nonexistent), and the proponents of Laetrile arguing that they are considerably better.

It must not be forgotten, moreover, that the measure of the value of Laetrile is not alone the high percentage of recovery from, or complete control of, the disease for which Laetrile can claim credit, as opposed to the lesser percentage attainable under state-sanctioned remedies, but the additional benefits which Laetrile offers, such as a certain but unmistakable diminution of pain, plus the offering to the patient of a course of treatment that avoids for him the hideous consequences of surgery, radiation, and/or chemotherapy.

In consideration of these realities, therefore, it can be reasonably argued that the reasons for imposing by law the state-sanctioned remedies, and for outlawing Laetrile, become so weak, that at this point the law's strong penchant for protecting the individual's right of privacy should be sufficient to tip the scales in favor of giving the patient his freedom of medical choice. Under the above circumstances, it can hardly be argued

that compelling and substantial reasons require giving the State-sanctioned remedies the status of an absolute monopoly.

The case for Laetrile is made even stronger since it can be established that it involves no toxicity whatsoever (in contradistinction to the State-sanctioned alternatives which involve a high degree of toxicity, or, in the case of surgery, bodily injury), and since the patient is acting under the direction of a personal physician who understands his needs far better than does the State, which can deal only in generalities, and which physician can be expected to take care of the State's interest in not allowing the patient to embark on a suicidal course, and since it can be clearly shown to be in society's best interest that more flexibility be given in the use of nontoxic drugs, to encourage that kind of generalized use which alone can resolve the baffling question of their efficacy.

It follows, therefore, that it becomes proper, at this point, to establish, from the record, and from other credible sources, that the Laetrile treatment can show a better record of recovery than can so-called State-sanctioned alternatives.

The District Court, when this case was first tried before it, found, as reported on page 1212:

The Court finds from the record, testimony and exhibits, that laetrile is not lethal in any sense of the word. It is not harmful to the human body and when used in proper amounts under proper control and supervision can effect relief from cancer disease to the satisfaction of many who are privileged to use the same.

During the second trial of this case in the District Court, Judge Bohanon found that not only was Laetrile's

safety not subject to the slightest doubt, but that a considerable array of competent physicians had already expressed themselves as favorable to its use. Admittedly, the overwhelming consensus among orthodox practitioners was against Laetrile. However, the weight to be given this negative consensus was considerably reduced, according to Judge Bohanon, by the fact that many of those who were most vociferous against Laetrile betrayed only a superficial familiarity with it, in contrast to its advocates, whose advocacy generally was born of familiarity with actual case histories of success.

The Court said, on page 1292:

Unquestionably, the administrative record in this case reveals a substantial and well-developed controversy among medical professionals and other scientists as to the efficacy of Laetrile.

Advocates of Laetrile's use in cancer treatment include many highly-educated and prominent doctors and scientists,<sup>9</sup> whose familiarity and practical experience with the substance vastly exceeds that of their detractors. To deem such advocacy "quackery" distorts the serious issues posed by Laetrile's prominence and requires disregarding considerable expertise mustered on the drug's behalf.

While the record reveals an impressive consensus among the nation's large medical and cancer-fighting institutions as to Laetrile's ineffectualness, a disconcerting dearth of actual experience with the substance by such detractors is revealed.

The footnote 9, referred to in the above quoted passage, reads as follows:

<sup>9</sup> Proponents of the use of Laetrile include:

Dean Burk, Ph.D. in biochemistry from the University of California. A research scientist possessing 35



years' experience with the National Cancer Institute, Dr. Burk is the former head of the Institute's Cytochemistry Section. (R. 302; Tr. 401).

Charles Gurhcot, Ph.D. in chemistry and physiology from the Cornell University, former assistant professor of Pharmacology, University of California Medical School at San Francisco. (R. 302 at J-206).

Chauncey D. Leake, Ph.D., former associate professor of pharmacology at University of Wisconsin (R. 302 at J-200).

Raymond Ewell, Ph.D. in chemistry from Princeton. (R. 302 at J-196).

Phillip Binzel, M.D., (Tr. 360); John A. Richardson, M.D. (R. 510, Ex. 1 and Tr. 462); The Honorable Lawrence R. McDonald, (R. 509); Ernst T. Krebs, Sr. M.D., and Dr. Ernst T. Krebs, Jr. (Tr. 228); perhaps as many as 600 American M.D.'s or more have employed and are advocating the use of Laetrile in cancer treatment (R. 313 at J-255).

David Rubin, M.D., surgeon at Beilinson Hospital and cancer researcher at Hadassah Hospital in Jerusalem, Israel. (R. 510, Ex. 12).

Mario Soto, M.D., of Mexico, authorized by the National Cancer Institute to conduct independent investigational studies with the Institute's cancer drugs. (R. 286, Tr. 478.)

Hans A. Nieper, M.D., Hanover, West Germany; Ernest Contreras, M.D., Tijuana, Mexico; Shigeaki Sakai, M.D.; of Tokyo, Japan; Ettore Guidetti, M.D. Brazil. (R 507).

Many doctors testify that Laetrile can confer an "improved quality of life" even upon patients who ultimately die, by reducing their pain and discomfort. For example, see P.E. Binzel, Fr., M.D., (Tr. 362); David Rubin, M.D. (R 510, Ex. 12).

There are even some members of the nation's leading cancer institutions who have voiced no objections to the use of Laetrile under proper circumstances. For example, at R 195 of the record transcript, appears an affidavit, referred to by Judge Bohanon in footnote 10, on page 1293, of C. Chester, Ph.D., vice-president and associate director for administrative and academic affairs of the Sloan-Kettering Institute for cancer Research, New York, in which he says: "I have stated before, . . . that if the patient has exhausted the benefits of conventional treatment and does not mind the financial outlay, I see no harm in his taking Amygdalin in the way it has generally been used."

Despite the assertion of the FDA that there are no known tests conducted on mice which show Laetrile to have had any positive results, the facts are that many such tests have been conducted showing positive results. Judge Bohanon, in footnote 13, page 1294 of his opinion, states:

Knowledgeable experts have expressed sharp criticism of certain prominent Laetrile tests on animals in which the substance was determined ineffective. Note the analyses of Dr. Bernard Kenton of the City of Hope National Medical Center, Los Angeles, California (R 507 at N 249); and Dr. Dean Burk (R302 at J-117); also those of Dr. Michael Fox, chairman of the Biomathematics Department of the City of Hope National Medical Center and assistant professor of biomathematics at UCLA, and Harold Hornsby, research scientist with NASA and a Fellow of the Royal Statistical Society in London (R 313 at J-253 and 254). Sloan-Kettering researcher Dr. Kanemasto Sugiura performed at least six different tests in which he concluded that Laetrile was effective in combatting certain types of

tumors; the Institute subsequently released other test results reportedly contradicting Dr. Sugiura's findings. Dr. Sugiura is quoted as saying: 'It is still my belief that amygdalin cures metastases'. (R 313 at J-241).

The California Court of Appeals, in the case of *People v. Privitera, supra*, on page 767, had this to say about the use of Laetrile to avoid the risks involved in conventional therapy:

Dr. Privitera points out that many cancer victims have investigated and evaluated the merits of surgery, radiation therapy, or chemotherapy with the aid of competent medical advice and have made the highly personal decision: The benefits from such therapy are not sufficient to justify the risks which include disfigurement, debilitation, and accelerated death, and for this reason have chosen to seek amygdalin as a treatment; other cancer victims have been advised that their condition is hopeless, their case is terminal and as a last resort before certain death, seek amygdalin.

Dr. Dean Burk, previously referred to, in his booklet "Vitamin B-17—a Brief on Foods and Vitamins", published by the Dean Burk Foundation, Inc., publication No. 1, 1975, reviews five carefully controlled experiments on mice that have shown definite Laetrile anticancer action. The following is quoted from his booklet, p. 15:

#### AMYGDALIN EFFICACY IN ANIMAL SYSTEMS

Anticancer vitamin activity by amygdalin (laetrile) has been observed in a wide variety of animal cancers, with high statistical significance, in more than five independent research institutions in three

widely separated countries of the world, including e.g.:

(1) Sloan-Kettering Cancer Center (New York), with CD<sub>8</sub>F<sub>1</sub> mice bearing spontaneous mammary carcinomas: inhibition of formation of lung metastases, inhibition of growth of primary tumors, and greater crystalline amygdalin/kg body weight/day (Report of K. Sugiura, June 13, 1975).

(2) Southern Research Institute (Birmingham, Alabama) for the National Cancer Institute, in a majority of 280 BDF<sub>1</sub> mice bearing Lewis lung cancers, treated with up to 400 mg crystalline amygdalin per kg body weight, with respect to increased life span (Report, December 3, 1974).

(3) Scind Laboratores, University of San Francisco, 400 rats bearing Walker 256 carcinoma (200 treated with amygdalin, 200 controls), with 80% increase in life span at optimum dosage (500 mg amygdalin/kg body weight) (October 10, 1968). Cf. FDA-IND application No. 6734. pp. 247-8, 00080-00093. NCI Director Carl Baker wrote Congressman Edwin W. Edwards on Jan. 26, 1971: "The data provided by the McNaughton Foundation certainly indicates some activity in animal tumor systems" (emphasis added).

(4) Pasteur Institute (Paris), with human cancer strain maintained in mice treated at optimal dosage of 500 mg Amygdalin Marson/kg body weight/day; increased life span and delayed tumor growth up to 100% (Dec. 6, 1971 report by M. Metianu).

(5) Institut von Ardenne (Dresden, Germany), H strain mice bearing Ehrlich ascites carcinoma treated with bitter almond amygdalin ad libitum in addition to the regular chow diet: increased life span and decreased rate of cancer growth, treatment

beginning 15 days before cancer inoculation (Arch. Geschwulstforsch. 42, 135-7 1973).

Dr. Hans Nieper, M.D. Director of the Department of Medicine at Silbersee Hospital in Hanover, Germany, who is listed in *Who's Who in World Science*, who is Director of the German Society of Medical Tumor Treatment, and who has had many years of personal experience with Laetrile (amygdalin), told newspaper reporters as long ago as 1972, the following:

After more than twenty years of such specialized work, I have found that non-toxic Nitrilosides—that is, Laetrile—are far superior to any other known cancer treatment or preventative. In my opinion it is the only existing possibility for the ultimate control of cancer.

In Canada, N.R. Bouziane, M.D., Director of Research Laboratories at St. Jeanne d'Arc Hospital in Montreal, member of the hospital's tumor board in charge of chemotherapy, a *magna cum laude* graduate in medicine from the University of Montreal, an affiliate of Oxford University in New Brunswick, a fellow in chemistry and a fellow in hematology, and certified in clinical bacteriology, hematology, and biochemistry from that college, after making a series of tests with Laetrile shortly after it was introduced, reported:

We always have a diagnosis based on histology [microscopic analysis of the tissue]. We have never undertaken a case without histological proof of cancer. . . .

In our investigation, some terminal cases were so hopeless that they did not even receive what we consider the basic dose of thirty grams. Most cases, however, became ambulatory and some have in this

short time resumed their normal activities on a maintenance dose. *Cancer News Journal*, Jan./April, 1971, p. 20.

In the Philippines Manuel Navarro, M.D., is professor of medicine and surgery at the University of Santo Tomas in Manila. He is an Associate Member of the National Research Council of the Philippines; a Fellow of the Philippine College of Physicians, and of the Philippine Society of Endocrinology and Metabolism; and a member of the Philippine Medical Association, the Philippine Cancer Society, and many other medical groups. He has over one hundred scientific papers to his credit, some of which have been read before the International Cancer Congress. In 1971 Dr. Navarro wrote:

I . . . have specialized in oncology [the study of tumors] for the past eighteen years. For the same number of years I have been using Laetrile-amygdalin in the treatment of my cancer patients. During this eighteen-year period I have treated a total of five hundred patients with Laetrile-amygdalin by various routes of administration, including the oral and the i.v. The majority of my patients receiving Laetrile-amygdalin have been in a terminal state when treatment with this material commenced.

It is my carefully considered clinical judgment, as a practicing oncologist and researcher in this field, that I have obtained most significant and encouraging results with the use of Laetrile-amygdalin in the treatment of terminal cancer patients, and that these results are comparable or superior to the results I have obtained with the use of the more toxic standard cytotoxic agents. *Cancer News Journal*, January/April, 1971, pp. 19, 20.



In Mexico, Ernesto Contreras, M.D., has operated the Good Samaritan Cancer Clinic in Tijuana for over a decade. He is one of Mexico's distinguished medical figures, having received postgraduate training at Harvard's Children's Hospital in Boston. He has served as Professor of Histology and Pathology at the Mexican Army Medical School and as the chief pathologist at the Army Hospital in Mexico City.

Dr. Contreras was introduced to Laetrile in 1963 by a terminal cancer patient from the United States, who urged him to treat her with it. The patient recovered, and so impressed Dr. Contreras, that he spent considerable time and effort in investigating Laetrile's properties. Since that time he has treated thousands of cancer patients, most of whom are American Citizens who have gone to Mexico to obtain what they were denied in the United States.

Dr. Contreras has summarized his experiences with vitamin (principally B-17) therapy as follows:

The palliative action [improving the comfort and well-being of the patient] is in about 60% of the cases. Frequently, enough to be significant, I see arrest of the disease or even regression in some 15% of the very advanced cases. *Cancer News Journal*, Jan./April, 1971, p. 20.

Dr. Shigeaki Sakai, a prominent physician in Tokyo, in a paper published in the October 1963 *Asian Medical Journal*, reported:

Administered to cancer patients, Laetrile has proven to be free from any harmful side-effects, and I would say that no anti-cancer drug could make

a cancerous patient improve faster than Laetrile. It goes without saying that Laetrile controls cancer and is quite effective wherever it is located.

In a recent statement, Arlin J. Brown, Director of the Arlin J. Brown Information Center, and a long-time student of cancer and its causes, said the following:

Laetrile is so effective in the prevention of cancer that no cases have ever been reported in individuals who ingest Laetrile and/or apricot kernels on a regular basis. . . . In the Asian country of Hunza . . . the average Hunzakut native normally consumed over 100 apricot kernels daily—and cancer is totally non-existent in that area. . . . The preventive nature of apricot kernels has also been scientifically demonstrated in the laboratory. Dr. Vern van Breeman, a biologist at Salisbury State College in Maryland, has shown that when mice, especially bred to develop cancer, are given apricot kernels, the cancer prevention rate is well over 90%. . . . All control mice developed cancer and died. Mice with leukemia lived 50% longer when given apricot kernels.

Dr. David Rubin, a surgeon and cancer researcher at Hadassah Hospital in Jerusalem, after 15 months of Laetrile research on terminal patients, stated:

The most striking observable feature was relief from pain accompanied by a decrease or even cessation of the need for pain killers and sleeping potions. In the majority of cases the patients came off long term use of narcotics without the usual withdrawal symptoms. After a few days of treatment with Laetrile there was an improvement in appetite, followed, in many cases, by a gain in weight. A frequent striking feature in

cancer wards is the odor of decaying cancer masses. We observed that this odor is generally absent in the cases under Laetrile therapy.

Testimonials favorable to Laetrile from other physicians are also readily obtainable. These include Professor Estore Guidetti, M.D., of the University of Turin Medical School, Italy; Professor Joseph H. Maisin, Sr. M.D., of the University of Louvain, Belgium, where he is Director of the Institute of Cancer; the late Dr. John A. Morrone of the Jersey City Medical Center, and many others.

The aforementioned Dr. Contreras, with his associates Drs. Abel Mellado Prince, and Dr. Jose Ernesto Contreras Pulido, recently analyzed retrospectively the charts on 1,200 cancer patients [most of whom were from the United States] to whom they had administered Laetrile. As indicated, most of them were in advance stages of cancer, i.e., were terminal cases. Only 1.1 percent had not received previous therapy.

The following report shows the results of their analysis:

#### AMYGDALIN. A NEW ANTI-TUMOR AGENT PHASE II STUDIES

DR. ERNESTO CONTRERAS RODRIGUEZ\*

DR. ABEL MELLADO PRINCE\*

DR. JOSE ERNESTO CONTRERAS PULIDO\*

**SUMMARY.** 1,200 charts of patients with proven

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\*From the Staff of Del Mar Medical Center and Hospital Playas de Tijuana, Baja Calif., Norte, Mexico.

malignant diseases were analyzed retrospectively. 32 different tumors were studied, the more frequent being rectum and colon (224 cases), lung (192 cases) and breast (180 cases). 86.7% of patients had extensive disease and tumor activity. Only 14 patients (1.1%) were received without previous therapy. All the patients received Amygdalin as the only anti-tumor agent for a minimum of 4 weeks and until—change of program or death. The subjective response was good in 65.1%, regardless of the stage and condition of the patients. Objective response was demonstrated in 32.6% of the cases. These were distributed as follows: Total remission 3.6%; partial remission 7.1%; improvements 12.3% and stabilizations 9.6%. The best responses were observed in carcinoma and lymphoma. Among the carcinomata, the best responders were bronchogenic, prostate, stomach and breast in postmenopausal women. These results, we believe, justify the clinical use of Amygdalin in advanced malignant disease. Prospective comparative studies (Phase III) should be planned for the more responsive tumors.

The said chart shows:

1. Practically all cancer patients treated had received previous therapy, and had gone to Laetrile, presumably because of their lack of faith or hope in the therapy previously received.
2. 86.7 percent had "extensive" disease and tumor activity.
3. Approximately 2/3 of the patients showed improved subjective response. In other words, they felt better.
4. Approximately 1/3 could show objective improvement.

5. Of that number, 3.6 percent showed total remission, and 7.1 percent partial remission; and 12.3 percent showed some improvement. Considering that these patients were presumably all terminal, 99 percent of whom had had previous treatment and were dissatisfied with the results, these results are impressive.

The number of cases where Laetrile has resulted in granting either a complete cure or a permanent "control" of the disease to cancer patients previously diagnosed as terminal, is impressive. No one knows the number, but it is far higher than can be explained on the theory of "spontaneous regressions". Dr. John A. Richardson, in his book "Laetrile Case Histories", (1977), discusses this point in the following language:

So, as a final resort, a last-ditch effort to discredit Laetrile, especially in those cases where there has been no prior orthodox therapy for the supposed delayed reaction, the critics finally fall back to the claim that these cases represent "spontaneous regressions," that the cancer just went away on its own, not as a result of Laetrile, but as a result of a return of the natural resistance of the host.

It is true that occasionally a patient will recover from cancer without any treatment whatsoever. This fact tells us something important. It tells us that the body *does* have some kind of *natural* control for the disease, if we only knew what it was. One thing is certain, whatever it is, it is *not* X-radiation or toxic chemicals.

The statistical probability for spontaneous regressions is just about the same as for delayed reactions. Most official estimates are 1 in 80,000 to 100,000 cases.<sup>7</sup> Warren Cole, Emeritus Professor of Surgery at the University of Illinois College of Medicine, reviewed the spontaneous remission cases reported in all the medical journals from 1960 to 1966. Including cases dating back to the early 1900's there were exactly 92 cases that had a survival rate of two years or more.<sup>8</sup>

If these really are cases of spontaneous remission, then it should be noted that I have more such cases at my own clinic than the rest of the world combined. It would seem that we get a much higher rate of "spontaneous remissions" using Laetrile than with anything else we've tried!

Ms. Gertrude Engel, previously referred to, in a prepared statement given before the Subcommittee on Health and Environment of the House Committee on Interstate and Foreign Commerce, on June 21, 1978, [which information was repeated before Senator Edward M. Kennedy, Chairman of the Senate Subcommittee on Health and Scientific Research] said the following:

Alicia Buttons, who was declared dying six years ago, also travels to Germany to receive treatment from D. Nieper. She is the wife of Red Buttons, famous actor comedian. I have been in constant touch with Alicia Buttons. I met them several years ago. Alicia was told she would pass away

<sup>7</sup>"Spontaneous Regression of Cancer: The Metabolic Triumph of the Host?" *Annals of the New York Academy of Science*, Vol. 230, op. cit. pp. 111, 112.

<sup>8</sup>*Ibid.*, p. 112.



because she had cancer of the lymph nodes, and Red Buttons took her to Germany to meet with Dr. Hans Nieper [for Laetrile treatment].

Mr. Buttons, in a public declaration to the world made just a few months ago, said, in this regard:

Six and a half years ago, . . . I got the news: "Red, your wife has cancer and it's very bad." The prognosis was: "With luck, she might be able to live a year."

That was six and a half years ago. I'm delighted to tell you that six and a half years after, my wife is fine and healthy and happy—thanks to something that has been condemned as a hoax and a fraud. That something is called LAETRILE.

Ms. Engel, in her aforementioned testimony before the House subcommittee, made two additional statements which are worthy of special note. First, she quoted Dr. Arthur Upton, who is Director of the National Cancer Institute, as follows: "There are, right now, in our files, over 200 cases of those people taking Laetrile, and very successfully."

She then quoted Dr. Donald Frederickson, Director of the National Institutes of Health, who said: "For the National Institutes of Health to say that Laetrile is worthless is wrong. We are trying to be objective."

In spite of the reluctance of Laetrile proponents to ever claim that Laetrile can invariably cure or control cancer, the fact remains that in many publicized and well-documented cases it has done just that. Some of these stories are deeply moving and highly dramatic. In spite of the reluctance of Laetrilists to build their case for Laetrile on the strength of these isolated, or, as the FDA calls them, "anecdotal" cases, their frequency seems to have defied every anti-Laetrile explanation. Various authors have from time to time, gathered together some of these stories, and they are easily available.<sup>9</sup>

As long as these exciting stories continue to be generated—stories that bring hope to otherwise despairing and condemned persons—and as long as a legal cloud still hovers over the use of Laetrile, there will remain a general disappointment which absolutely nothing that the law can do, other than the complete legitimizing of Laetrile, can ever hope to dispel.

Laetrilists are not dogmatists. It would seem prudent to grant to the use of Laetrile the same room for growth and development as has been so assiduously reserved by the law for other treatments which have now (but had not at the beginning), attained respectability.

It must also be recalled that the success or failure of the Laetrile treatment depends in large measure on associated factors such as: the willingness of the patient

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<sup>9</sup>See, for example, "Laetrile Case Histories" by John A. Richardson, M.D. and Patricia Griffin, R.N., previously referred to.

to submit to a rigid dietary regime, the ingestion of other vitamins and enzymes, etc. Doctors are more and more realizing that the restructuring of a patient's metabolic system involves a multitude of factors, of which only one, albeit an important one, is the ingestion of heavy concentrations of vitamin B-17.

At the second trial of this case before Judge Bohanon, P.E. Binzel, Jr., M.D., testified, (tr. 363):

I know of no doctor throughout the world who is now using Amygdalin who does not agree that the maximum benefit from Amygdalin is obtained when it is used in combination with other vitamins, enzymes, and proper diet.

In spite of the FDA's intense antagonism to Laetrile, and to the medical rationale underlying it, it is interesting to note, here and there, a begrudging concession by the FDA to some of the Laetrilists' major premises. For example, with regard to the premise that cancer is related to dietary deficiency, and particularly vitamin deficiency, (which is one of Laetrilists's major theses), we read, in the FDA's publication "The Cancer Story", 1973 revision, on page 34, the following:

There is some evidence that vitamin deficiency in man plays a role in the occurrence of cancers of the oral cavity and the esophagus. . . If such deficiency exists, it is probably only one of a number of factors to be considered.

Regarding another of Laetrilists' premises, namely that the body can develop its own system of immunity, the aforementioned "The Cancer Story", on page 46, has the following statement:

Closely allied to virus research are advances in immunology. We know that many cancers manufacture antigens, to which the body reacts by

humeral and cellular immune responses. . . Knowledge in tumor immunology is being rapidly applied to the diagnosis and treatment of cancer.

We now address the disappointing record of so-called state-sanctioned cancer treatments: surgery, radiation, and chemotherapy. Stripped of the latter's aura of respectability, with which time and institutionalization have vested them, their record of success must be recognized as appalling.

Laetrile's record of success, though far from perfect, must not be judged in a vacuum. Any meaningful evaluation must be in the nature of a comparison with available alternatives. Such a comparison leaves Laetrile in by far the better position.

Judge Bohanon addressed this question in footnote 25 on page 1299 of his opinion, as follows:

Such a decision [to have recourse to Laetrile] is by no means necessarily indicative of suicidal tendencies. Dr. Hardin Jones of the University of California has presented impressive evidence in support of the thesis that in some instances at least untreated cancer victims outlive treated ones. (R 507) Conventional modes of treatment, particularly radiation and chemotherapy, can cause extensive damage to healthy organs and tissues as well as cancerous ones. Some argue that in destroying the body's natural defense mechanisms such approaches often destroy important weapons crucial to an effective fight against cancer and also greatly increase a patient's vulnerability to other life-threatening diseases as well.

Patients possessing particularized complicating factors, such as old age, frail physical constitutions, or certain types of religious convictions, might also understandably decide to forego the rigors of such conventional methodologies.

Even doctors who oppose the use of Laetrile will generally concede as to orthodox modes of treatment (surgery, radiation and chemotherapy): "... the treatments that are available are very often disfiguring; they can be painful; they can be unpleasant; they can even be risky." Emil J. Freireich, Professor of Medicine at the University of Texas, School of Medicine, Houston. (Tr. 204)

In attacking the credibility of "cures" reported to have been effectuated by Laetrile, FDA argues that in many such instances the person involved may never even have had cancer. "Even where the diagnosis has been done by someone other than a Laetrile proponent, a mistake is possible. Some cancers which are discussed in reference to Laetrile are very difficult to diagnose histologically. Thus, a diagnosis of cancer may often on later review be reversed." Commissioner's Decision (R 523) at 227). This analysis is hardly reassuring to individuals such as plaintiff Glen Rutherford, whose proposed surgery, a colostomy, would have unalterably lessened the quality of his life, irrespective of the ultimate outcome of his illness. (See *Rutherford v. United States*, 399 F. Supp. 1208 (W. D. Okl.1975).

In the volume "World without Cancer", by G. Edward Griffin, 1977 printing, starting on page 172, we read:

For comparison let us take a look at the results and benefits of the so-called cures obtained through surgery, radiation, and chemotherapy.

As we shall see, surgery is the least harmful of the three. In all fairness it must be said that, in some cases, it can be a life-saving stop-gap measure—particularly where intestinal blockages and adhesions must be relieved in order to prevent the

patient from dying from secondary complications. Surgery also has the psychological advantage of visibly removing the tumor. And, from that point of view, it offers the patient and his family some temporary comfort and hope. However, the degree to which surgery is useful is the same degree to which the tumor is *not* malignant. The greater the proportion of cancer cells in that tumor, the less likely it is that surgery will help. And the most highly malignant tumors of all generally are considered inoperable.

A further complication of surgery is the fact that any cutting into the tumor—even a biopsy—does at least two things that logically should aggravate the condition. First, it causes physical trauma to the area. . . The other effect is that, if not all the malignant tissue is removed, what remains tends to be encased in scar tissue from the surgery. Scar tissue tends to act as a barrier between the cancer cell and the rest of the body . . .

Perhaps the greatest indictment of all against surgery is the knowing suspicion among even many of the world's top surgeons that, statistically, there is no solid evidence that patients who submit to surgery have any greater life expectancy on the average, than those who do not. This is an area which desperately needs intensive and unbiased study.

The first statistical analysis of this question was compiled in 1844 by Dr. Leroy d'Etoilles and published by the French Academy of Science. It is, to date, the most extensive study of its kind ever released. Over a period of thirty years, case histories of 2,781 patients were submitted by 174 physicians. The average survival after surgery was only one year and five months—not much different than the average today.



Dr. Leroy d'Etoilles separated his statistics according to whether the patient submitted to surgery or caustics, or refused such treatment. His findings were electric:

The net value of surgery or caustics was in prolonging life two months for men and six months for women. But that was only in the first few years after the initial diagnosis. After that period, those who had not accepted treatment had the greater survival potential by about fifty percent.<sup>1</sup> [Footnotes to Griffin material appear on p. 61]

1844, of course, was a long time ago. But recent surveys invariably have produced nearly the same results. For instance, it long has been accepted practice for patients with breast cancer to have not only the tumor removed but the entire breast and the lymph nodes as well. In more recent years, the procedure often includes removal of the ovaries also on the theory that cancer is stimulated by their hormones. Finally, in 1961, a large-scale controlled test was begun, called the National Surgical Adjuvant Breast Project. After seven-and-a-half years of statistical analysis, the results were conclusive: There was no significant difference between the percentage of patients remaining alive who had received the smaller operation and those who had received the larger.<sup>2</sup>

One of the most distinguished statisticians in the medical field is Hardin B. Jones, Ph.D., professor of medical physics and physiology at the University of California at Berkeley. After years of searching published and unpublished clinical records, he appeared at an American Cancer Society convention and reported bluntly:

In regard to surgery, no relationship between intensity of surgical treatments and duration of survival has been found in verified malignancies.

On the contrary, simple excision of cancers has produced essentially the same survival as radical excision and dissection of the lymphatic drainage.<sup>3</sup>

All of this, of course, related only to surgery of the breast. Turning his attention to surgery in general, Dr. Jones reported:

Although there is a dearth of untreated cases for statistical comparison with the treated, it is surprising that the death risks of the two groups remain so similar. In the comparisons it has been assumed that the treated and untreated cases are independent of each other. In fact, that assumption is incorrect. Initially, all cases are untreated. With the passage of time, some receive treatment, and the likelihood of treatment increases with the length of time since origin of the disease. Thus, those cases in which the neoplastic process progresses slowly [and thus automatically favors a long-term survival] are more likely to become "treated" cases. For the same reason, however, those individuals are likely to enjoy longer survival, whether treated or not. Life tables truly representative of untreated cancer patients must be adjusted for the fact that the inherently longer-lived cases are more likely to be transferred to the "treated" category than to remain in the "untreated until death."

*The apparent life expectancy of untreated cases of cancer after such adjustment in the table seems to be greater than that of the treated cases.*

[Emphasis added]

What, then, is the statistical chance for long-term survival of five years or more after surgery? That, we are told, depends on the location of the

cancer, how fast it is growing, and whether or not it has spread to a secondary point in the body. For instance, two of the most common forms of cancer requiring surgery are of the breast and the lung. In the case of breast cancer, only sixteen percent will respond in any way to either surgery or X-ray therapy. In the case of lung cancer, the percentage of patients who will survive five years after surgery is somewhere between five and ten percent.<sup>4</sup> And these are optimistic figures when compared to survival expectations for some other types of cancers such as testicular chorionepitheliomas.

An objective appraisal, therefore, is that the statistical rate of long-term survival after surgery is, on the average *at best*, only ten or fifteen percent. And once the cancer has metastasized to a second location, surgery has almost *no* survival value whatsoever. The reason, of course, is that, like the other therapies approved by orthodox medicine, surgery removes only the tumor. It does not remove the cause.

The rationale behind X-ray therapy essentially is the same as with surgery. The medical objective is to remove the tumor, but to do so by burning it away rather than cutting it out. Here, also, it is primarily the non-cancer cell that is destroyed. The more malignant the tumor, the more resistant it is to radio therapy. This should be obvious for, if it were the other way around, then X-ray therapy would have a high degree of success—which, of course, it does not.

If the average tumor is composed of both cancer and non-cancer cells, and if radiation is more destructive to non-cancer cells than to cancer cells, then it would be logical to expect the results to be

a *reduction* of tumor *size*, but also an *increase* in the *percentage of malignancy*. This is, in fact, exactly what happens.

Commenting on this mechanism, Dr. John Richardson has explained it this way:

Radiation and/or radiomimetic poisons *will* reduce palpable, gross or measurable tumefaction. Often this reduction may amount to seventy-five percent or more of the mass of the growth. These agents have a selective effect—radiation and poisons. They selectively kill everything except the definitively neoplastic [cancer] cells.

For example, a benign uterine myoma will usually melt away under radiation like snow in the sun. If there be neoplastic cells in such tumor, these will remain. The size of the tumor may thus be decreased by ninety percent while the relative concentration of definitively neoplastic cells is thereby increased by ninety percent.

As all experienced clinicians know—or at least should know—after radiation or poisons have reduced the gross tumefaction of the lesion the patient's general well-being does not substantially improve. To the contrary, there is often an explosive or fulmination increase in the biological malignancy of his lesion. This is marked by the appearance of diffuse metastasis and a rapid deterioration in general vitality followed shortly by death.<sup>5</sup>

And so we see that X-ray therapy is cursed with the same limitations and drawbacks of surgery. But it also has one more: it actually increases the likelihood that cancer will develop in other parts of the body!

Yes, it is a well-established fact that excessive exposure to radioactivity is an effective way to induce cancer. This was first demonstrated by observing the increased cancer incidence among the survivors of Hiroshima, but it has been corroborated by many independent studies since then. For example, a recent headline in a national circulation newspaper tells us: FIND ALARMING NUMBER OF CANCER CASES IN PEOPLE WHO HAD X-RAY THERAPY 20 YEARS AGO.<sup>6</sup>

The *Textbook of Medical Surgical Nursing*, a standard reference volume for Registered Nurses, is most emphatic on this point. It says:

This is an area of public health concern because it may involve large numbers of people who may be exposed to low levels of radiation over a long period of time. The classic example is of the women employed in the early 1920's to paint watch and clock dials with luminizing (radium-containing) paints. Years later, bone sarcomas resulted from the carcinogenic effect of the radium. Similarly, leukemia occurs more frequently in radiologists than other physicians. Another example is the Hiroshima survivors who have shown the effects of low levels of radiation. . .

Now to the question of statistics. Again we find that, on the average, there is little or no solid evidence that radiation actually improves the patient's chances for survival. The National Surgical Adjuvant Breast Project, previously mentioned in connection with surgery, also conducted studies on the effect of irradiation, and here is a summary of their findings:

From the data available it would seem that the use of post-operative irradiation has provided

no discernible advantage to patients so treated in terms of increasing the proportion who were free of disease for as long as five years.<sup>7</sup>

This is an embarrassingly difficult fact for a radiologist to face, for it means, quite literally, that there is little real justification for his existence in the medical fraternity. If he were to admit publicly what he knows privately from experience, a guy could talk himself right out of a job! Consequently, one does not expect to hear these facts being discussed by radiologists or those whose livelihood depends on the construction, sale, installation, use, or maintenance of the multi-million dollar linear accelerators. It comes as a pleasant surprise, therefore, to hear these truths spoken frankly and openly by three well known radiologists sharing the same platform at the same medical convention. They were William Powers, M.D., Director of the Division of Radiation Therapy at the Washington University School of Medicine, Philip Rubin, M.D., Chief of the Division of Radiotherapy at the University of Rochester Medical School, and Vera Peters, M.D., of the Princess Margaret Hospital in Toronto, Canada. Dr. Powers states:

Although preoperative and postoperative radiation therapy have been used extensively and for decades, it is still not possible to prove unequivocal clinical benefit from this combined treatment . . . Even if the rate of cure does improve with a combination of radiation and therapy, it is necessary to establish the cost in increased morbidity which may occur in patients without favorable response to the additional therapy.<sup>8</sup>

Dr. Rubin's statement was even more to the point. After reviewing the statistics of survival previously published in the *Journal of the American Medical Association*, he concluded:



The clinical evidence and statistical data in numerous reviews are cited to illustrate that no increase in survival has been achieved by the addition of irradiation.

To which Dr. Peters added:

In carcinoma of the breast, the mortality rate still parallels the incidence rate, thus proving that there has been no true improvement in the successful treatment of the disease over the past thirty years, even though there has been technical improvement in both surgery and radiotherapy during that time.

Or, putting it even more succinctly, Dr. Irwin H. Krakoff, of the Sloan-Kettering Institute for Cancer Research, says simply:

We are concerned with a disease for which there is no really satisfactory treatment.<sup>9</sup>

In view of all this, it is exasperating to find spokesmen for orthodox medicine continually warning the public against using Laetrile on the grounds that, supposedly, that will prevent the cancer patient from benefiting from "proven" cures.

Battling as a lone warrior within the enemy stronghold, Dr. Dean Burk of the National Cancer Institute repeatedly has laid it on the line. In a letter to his boss, Dr. Frank Rauscher, he said:

In spite of the foregoing evidence, . . . officials of the American Cancer Society and even of the National Cancer Institute, have continued to set forth to the public that about one in every four cancer cases is now "cured" or "controlled," but seldom if ever backed up with the requisite statistical or epidemiological support for such a statement to be scientifically meaningful, however effective for fund gathering. Such a state-

ment is highly misleading, since it hides the fact that, with systemic or metastatic cancers, the actual rate of control in terms of the conventional five-year survival is scarcely more than one in twenty. . .<sup>10</sup>

<sup>1</sup>Walshe, Walter H., *The Anatomy, Physiology, Pathology and Treatment of Cancer*, (Ticknor & Co., Boston, 1844).

<sup>2</sup>Ravdin, R.G., et al., "Results of Clinical Trial Concerning the Worth of Prophylactic Oophorectomy for Breast Carcinoma," *Surgery, Gynecology & Obstetrics*, 131:1055, Dec., 1970. Also see "Breast Cancer Excision Less with Selection," *Medical Tribune*, Oct. 6, 1971, p. 1.

<sup>3</sup>"A Report on Cancer," paper delivered to the ACS's 11th Annual Science Writers Conference, New Orleans, Mar. 7, 1969.

<sup>4</sup>See "Results of Treatment of Carcinoma of the Breast Based on Pathological Staging," by F.R.C. Johnstone, M.D., *California Medical Digest*, Aug., 1972, p. 839. Also, "Consultant's Comment," by George Crile, Jr., M.D. *Surgery Gynecology & Obstetrics*, 134:211, 1972. Also "Project aims at Better Lung Cancer Survival," *Medical Tribune*, Oct. 20, 1971. Also statement by Dr. Lewis A. Leone, Director of the Department of Oncology at Rhode Island Hospital in Providence, as quoted in "Cancer Controls Still Unsuccessful," *L.A. Herald Examiner*, June 6, 1972, p. C-12.

<sup>5</sup>Open letter to interested doctors, Nov., 1972.

<sup>6</sup>The National Enquirer, Oct. 7, 1973, p. 29.

<sup>7</sup>Fisher, B., et al., "Postoperative Radiotherapy in the Treatment of Breast Cancer; Results of the NSAPP Clinical Trial," *Annals of Surgery*, 172, No. 4, Oct. 1970.

<sup>8</sup>"Preoperative and Postoperative Radiation Therapy for Cancer," speech delivered to the Sixth National Cancer Conference, sponsored by the American Cancer Society and the National Cancer Institute, Denver, Colorado, Sept. 18-20, 1968.

<sup>9</sup>Speech delivered before the American Society of Clinical Oncology in 1968.

<sup>10</sup>Letter to Congressman Frey. op. cit.

With regard to the use of chemotherapy, the results are equally unsatisfactory. Dr. John Trelford of the Department of Obstetrics and Gynecology at Ohio State University Hospital has said:

At the present time, chemotherapy of gynecological tumors does not appear to have increased life expectancy except in sporadic cases . . . The problem of blind chemotherapy means not only a loss of the effect of the drugs, but also a lowering of the patient's resistance to the cancer cells owing to the toxicity of these agents.<sup>10</sup>

Dr. Saul A. Rosenberg, Associate Professor of Medicine and Radiology at Stanford School of Medicine, said, with regard to cancer chemotherapy:

Worthwhile palliation is achieved in many patients. However, there will be the inevitable relapse of the malignant lymphoma, and, either because of drug resistance or drug intolerance, the disease will recur, requiring modifications of the chemotherapy program and eventually failure to control the disease process.<sup>11</sup>

Dr. Charles Moertel of the Mayo Clinic had this to say on the subject of chemotherapy:

Our most effective regimens are fraught with risks and side-effects and practical problems; and after this price is paid by all patients we have treated, only a small fraction are rewarded with a transient

<sup>10</sup>"A Discussion of the Results of Chemotherapy on Gynecological Cancer and the Host's Immune Response." Sixth National Cancer Conference proceedings.

<sup>11</sup>"The Indications for Chemotherapy in the Lymphomas," Sixth National Cancer Conference proceedings.

period of usually incomplete tumor regression . . . Our accepted and transitional curative efforts, therefore, yield a failure rate of 85% . . . Some patients with gastrointestinal cancer can have very long survival with no treatment whatsoever.<sup>12</sup>

The FDA argues strenuously that trafficking in Laetrile carries with it the danger that people might be misled into subscribing to unsatisfactory cures. If the unsatisfactory results from state-sanctioned cancer remedies were actually known to the general public, it is not unreasonable to conclude that the feeling would be that the misleading has been in the other direction.

**C. Laetrile is destined only for Informed, Consenting, Adult, Terminal Cancer Patients Acting Under the Direction of Competent Physicians, and is to be Administered by said Physicians to the said Patients, and to none Else.**

The essence of FDA's argument is that it serves a valid State purpose for the State to proscribe trafficking in Laetrile, in that Laetrile has not yet received an approved new drug application, which means that its efficacy has not yet been adequately demonstrated according to legal standards. Therefore, since the possibility exists that Laetrile may not be effective, the state should protect the public therefrom, for the same reason that it protects citizens from all other drugs not yet proven to be effective.

It must be remembered, however, that Laetrile is not a non-prescription drug. No one contends that it should be placed in the over-the-counter category, where protection

<sup>12</sup>Speech made at the National Cancer Institute Clinical Auditorium, May 18, 1972.

to the public against ineffective drugs becomes particularly important. Laetrile is furnished on prescription and will be administered by a doctor who is acquainted with the patient, and the characteristics of his illness. The doctor has spent many years preparing himself for this responsibility, and has been certified by the State as a person qualified to prescribe and administer treatments according to his best judgment. In many cases, these doctors have had years of experience with Laetrile, and have seen its reaction on hundreds of terminal cancer patients. Under the circumstances it is difficult to conclude that a sufficiently substantial and compelling state interest is served—sufficient, in fact, to justify depriving the patient of his constitutional right of privacy—to take the choice of therapy away from the State's own licensed physician, and give it to a board, whose members have had no experience with Laetrile, and who know nothing about the patient. It must be remembered, moreover, that no question of toxicity is here presented. It has already been demonstrated in this brief that the State-approved alternatives are *very* toxic, in contrast to Laetrile, whose record is one of complete non-toxicity.

It must also be remembered that we are not concerned, here, with selling or promoting the sale of Laetrile to uninformed persons. There is no misrepresentation, no fraud, no snake-oil artistry, no quackery. The Laetrile-consumer is an adult, informed, consenting, cancer patient, acting under the direction and at the recommendation of his own personal physician. Where is the great State purpose which demands a disruption of this arrangement?

The California Court of Appeals, in the case of *People v. Privitera*, *supra* at page 781, said:

The doctor in California is licensed to practice only after meeting long rigid education, experience qualifications. He is bound by oath to preserve, to prolong, the life of his patient. He is under a legal duty, under threat of malpractice suit, to act in accordance with the generally accepted standards of medical practice in his community in this state. He is required under threat of malpractice to treat only after receiving the informed consent of the patient. (*Cobbs v. Grant*, *supra*, 8 Cal. 3d 229, 104 Cal. Repr. 505, 502 p.2d 1.) These are the "rational means" society through law has imposed to insure a high standard of performance by the California doctor. It follows after such rigid standards are met, the matter of choice of treatment of the informed consenting patient becomes "a purely medical determination, which is within a doctor's professional judgment." (*Aden v. Younger*, *supra*, 57 Cal. App. 3d 662, 677, 129 Cal. Rptr. 535, 545.)

"Reliance must be placed upon the assurance given by his license, . . . that he possesses the requisite qualifications." (*Dent v. State of West Virginia*, 129 U.S. 114, 122-123, 9 S. Ct. 231, 233, 32 L. Ed. 623.)

Limiting this exercise of the doctor's professional judgment on some vague suspicion that "various persons" in this state are engaging in quackery does not follow as a matter of logic.

The premise that "various persons,"—conman, snake oil salesman,—have made or will make false and misleading representations to the public concerning the diagnosis, treatment and cure of cancer certainly warrants, as a rational means, the law which prohibits and makes criminal such acts. Health and Safety Code section 1714 accomplishes



this precise purpose. It prohibits a false representation with intent to defraud of any device or substance or treatment as an effective cure for cancer. Dr. Privitera does not contest the appropriateness of Health and Safety Code section 1714 as it does fit the announced legislative purpose.

**D. There is no Rational Relationship between the alleged Compelling State Purpose of Discouraging Recourse to non-State-Approved Alternative Treatments, and the Means Employed to Accomplish this Purpose, viz., the Proscription Placed (1) on the Importation of Laetrile, or (2) on its Transportation in Interstate Commerce.**

So much has been said in this brief on this point that little need here be added. If this case involved a situation where: 1) the state-prescribed treatments were clearly effective; 2) the state non-prescribed alternatives were clearly ineffective; 3) the patient was acting on his own, without knowledge, and without professional guidance; and 4) the proscription of Laetrile did actually succeed in discouraging cancer patients from having recourse to ineffective and unsanctioned remedies at the expense of effective state-sanctioned alternatives, then the FDA would have a strong case. The facts, however, are exactly the opposite of the above in each case. The state-prescribed treatments are of very limited effectiveness. There is very substantial evidence to indicate that the state non-prescribed alternative (Laetrile) is more effective than the state-prescribed treatment, at least in a great number of instances, in prolonging life. Its record, moreover, for reducing pain is excellent. The Laetrile patient is informed, and acts under the direction of a competent physician. Finally, the action of the FDA

has *not* cut down the use of Laetrile. All it has done is to force perhaps hundreds of thousands of patients to go to Mexico, or to Canada, or to Germany, or elsewhere, to submit to the latter's treatment at great cost to themselves. In almost every case, as has been previously pointed out, these patients have already submitted to state-sanctioned treatments, which have failed. That is why they have opted for Laetrile.

Moreover, the action of the FDA has had exactly the wrong effect: It has driven Laetrile underground; it has developed a black market for it and raised its prices; it has increased the patient's expenses at a time when he could least afford it; it has made lawbreakers out of honest citizens; it has taken much of the manufacture of Laetrile out from under the supervision of the FDA for purposes of ensuring good manufacturing practices, and purity of quality, and has thus encouraged inferior-quality production; and, finally, it has discouraged the sharing of information about it, and has made it extremely difficult to accomplish what everyone wants accomplished: namely, the obtaining of empirical confirmation of Laetrile's claims.

The Court cannot fail to find it of great interest that as of this date, nineteen states have already enacted legislation specifically approving and legalizing the administration of Laetrile to cancer patients by a licensed physician. All this has occurred within approximately the last three years. Many more states will probably add themselves to the nineteen. What will be the position of a terminal cancer patient then, who feels that he is dying because of his inability to procure Laetrile (because of the proscription on its interstate transportation), but who is residing in a state which sanctions it but cannot produce it (Alaska, for example)? What will happen if and

when a substantial portion of the states (or perhaps all of them) legalize Laetrile, and the FDA continues to proscribe its transportation in interstate commerce?

## II.

**LAETRILE IS NOT A NEW DRUG FOR THE REASONS (AMONG OTHERS) THAT IT IS EXEMPT BY VIRTUE OF THE PROVISIONS OF SECTION 107 OF PUB. L. 87-781.**

*Amicus* adopts the argument of Judge Bohanon, *in toto*, on this point (Point IV, pp. 1294 through 1298 of his opinion).

## III.

**WHEN APPLICABLE TO AN INFORMED CONSENTING TERMINAL CANCER PATIENT, THE TESTS OF "SAFETY" AND "EFFECTIVENESS", AS PROVIDED BY SECTION 201(p)(1) OF THE ACT (21 U.S.C. 321(p)(1), HAVE NO MEANING IN THE ABSENCE OF SPECIAL STANDARDS APPLICABLE TO THOSE CIRCUMSTANCES.**

*Amicus* adopts the arguments of Judge Seth, of the Tenth Circuit Court of Appeals, covering this point insofar as it applies to safety. In the absence of special standards, the test of "safety" cannot be rationally applied to terminal cancer patients. *Amicus* contends that terminal cancer patients are as entitled to "safe" drugs as any other patient, but that rational standards must be formulated according to which the test can be applied. However, in view of the fact that the District Court found from the record that Laetrile was generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as being safe, and thus meeting the requirements of the exemption provided in section 201(p)(1) of the Act, 23 U.S.C. 321(p)(1), since Laetrile is therefore not a new drug, the consideration of this point is moot.

## CONCLUSION

*Amicus* does not challenge the right of the State to administer public health programs, and, through the exercise of its police power, to protect human life, even to the point of prohibiting self-destruction. The position of this brief, however, is that the exercise of such right and power must be subject to reasonable limitations, lest the absurdities created by an unreasonable application thereof result in violating the correlative right guaranteed to each individual to regulate his own life. The latter right is just as sacred as the right of the State to prevent him from destroying his life.

In the instant case, the arguments favoring the State's exercising its police power to withhold Laetrile from the plaintiff and those in his class, seem out of touch with reality. We are not dealing here with protecting an uninformed sick person from the blandishments of an unprincipled promoter of quack remedies. Rather we are dealing with a terminal cancer patient who has probably had little else on his mind for months—perhaps years. He has placed himself in the care of a physician, and has discussed the matter with him. The latter has recommended Laetrile—probably as a last resort, after all else has failed. The patient has been told that he stands a good chance of being relieved from his pain and suffering. He is told that although no one can promise him a "cure", or even a remission, the past record of Laetrile does show a number of recoveries by patients who had previously been characterized as hopeless.

If such a patient, knowing all the facts and risks, elects to take a course of action recommended to him by the physician in whom he has placed confidence, can it be said that such a decision is so egregiously irrational

that the State has a duty to intervene, and to forbid him to carry out his own desires?

The State's position would be more convincing if its proffered alternatives had a better record. The success record of these alternatives is notoriously poor. In view of this fact, no rational person could question the need to expand our knowledge of cancer on every front. Science should not fear to initiate new approaches where old ones have proven barren. To do this, however, a reasonable flexibility in administering the Act is imperative. An unrealistic and unnecessarily-rigid application of its restrictions will result in "locking in" all the present modalities, and locking out all the new, and competing ones. But this is the very result which society must repugn.

If society is ever to conquer the monster cancer, it will be by encouraging scientists to tread paths that have never been trodden before. *This will not be accomplished by imposing more fines, more prison sentences, more restrictions.* It will be accomplished by granting a reasonable flexibility to the law's administration, to the end that needed protection may be assured, on the one hand, and innovation encouraged, on the other. For this reason, *Amicus* asks this honorable Court to decree that the injunction issued by the trial court be made permanent.

Respectfully submitted,

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No. 78-605

Supreme Court, U. S.  
FILED

APR 9 1979

MICHAEL RODAK, JR., CLERK

**In the  
Supreme Court of the United States**

OCTOBER TERM, 1978

UNITED STATES OF AMERICA, et al.,

*Petitioners,*

vs.

GLEN L. RUTHERFORD, et al.,

*Respondents.*

On Writ Of Certiorari To The United States Court  
Of Appeals For The Tenth Circuit

**BRIEF, AMICUS CURIAE, IN SUPPORT OF  
RESPONDENTS, OF CANCER  
CONTROL SOCIETY**

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**BRIEF, AMICUS CURIAE, IN SUPPORT OF  
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**The Cancer Control Society and Laetrile**

The Cancer Control Society is a California not-for-profit corporation, and its membership is comprised of thousands of men and women, approximately 50% of which are either present or former cancer victims, or members of their immediate families are such. The Society publishes scientific



information from both orthodox and other sources, performs research into cancer therapies available in the U. S. and elsewhere, and maintains up-to-date information as to where cancer sufferers may seek relief, when so often ineffective conventional cancer treatment has been of no avail. Its members believe that health freedoms are inherently guaranteed to us as human beings.

The Society opposes monopoly and compulsion in matters related to cancer therapies, and its membership believes in the "freedom of choice" now, and always, exercised by American citizens as to their health, and opposes bureaucratic dictation in health matters, of any type whatsoever from Washington, D.C., or elsewhere. The Society urges that freedom encompasses the freedom of the terminally ill, members of the respondent class, and, in fact, everyone to choose between existing therapies for the treatment of cancer. The Society also believes that such choice between highly toxic and largely ineffective orthodox cancer therapies, and non-toxic therapy of treatment with Laetrile, as included in an overall "metabolic therapy" program, lies within the Constitutionally protected right of privacy, allowing members of the Respondent class, and others, to make said choice free from governmental intervention or dictation.

### **The Rulings of the U. S. District Court**

Heretofore the U. S. District Court for the District of Oklahoma, Honorable Luther Bohanon presiding, has ruled extensively concerning the legal status of Laetrile, these rulings having followed a so-called "rule-making" proceeding of FDA, previously ordered by the U. S. Court of Appeals for the Tenth Circuit and the U. S. District Court in prior rulings.

The December, 1977 opinion of the District Court (Pet. App. 11-44A) is reported at 438 F. Supp. 1287.

The U. S. District Court ruling was, in summary:

1. That Laetrile, on October 9, 1962 (and, therefore, thereafter) was "generally recognized as safe" and met the other criteria of the 1962 "Grandfather Clause" to the Federal Food, Drug, and Cosmetic Act, and therefore is a drug proper and legal for distribution in interstate commerce.

2. That there is a Constitutional "right of privacy" which attaches to Respondent Glen Rutherford, and the others of the class action group of plaintiffs who have brought the within action, as well as to those not specifically members of that class, which bars FDA from interfering with their use of Laetrile.

The Society considers the U. S. District Court opinion and ruling in question to be well-reasoned, exhaustive and definitive in all respects, and it deems it superfluous at this point to amplify or further discuss the same. The Society adopts the ruling of said lower Court in all respects as though set forth herein in full in this amicus curiae brief.

The Society further notes to the Court that FDA herein does not seek to limit availability of Laetrile to terminal cancer patients, or even any other designated class of persons, but by the ruling it seeks from this Court would bar Laetrile to everyone, no matter what their position or condition.

If the petitioner agency is successful herein in its plea to the Court, namely that no one, not even a terminal cancer patient, may receive Laetrile in any form, thousands of patients now dependent upon Laetrile, and presently pro-

ected by the decrees of the District Court below and the 10th Circuit U. S. Court of Appeals, will be effectively left to die without the treatment they now value for their very lives.

### **Cancer — A National Disaster**

The petitioner agency unjustifiably seeks to "gloss over", so to speak, the depressing national cancer statistics, imputing to this Court that with orthodox, or conventional, cancer therapies, we are "winning" in the battle against cancer. Therefore, according to FDA reasoning, Laetrile could not possibly be desired by anyone. Petitioner even includes in its brief (page 73) "statistics" designed to buttress this argument. However, and interestingly enough, these are not U. S. Government statistics, but gleaned from a medical journal article not substantiated in the record herein.

Whatever the case, we are losing 400,000 Americans per year from cancer, with the mortality rate steadily increasing. If present projections are taken into account, one in four Americans is doomed to die of cancer. The *cancer death rate* has more than trebled since 1900, and the median survival time (based upon approximately 219,500 cases of cancer) is only *1.7 years*. The death rate for distant or disseminated cancer cases over a five-year period is *91%*.

Small wonder that terminal cancer patients like Respondent Rutherford, and others, desire Laetrile to prolong their lives, and even help them back to health, when orthodox therapy is totally ineffectual.

### **Orthodox Therapy — Ineffectual and Dangerous**

The Food and Drug Administration has a long history of allowing dangerous and worthless cancer drugs on the market, and its opposition to Laetrile is inexplicable under the circumstances at hand, wherein for very minor rea-

sons, the Agency seeks to challenge the "safety" of Laetrile, as contrasted with purportedly "safe" cancer drugs already approved by the Agency. The Society trusts that this attempt to create a "double standard" as applied to Laetrile shall not be permitted by the Court.

Presumably FDA seeks to justify its approval of drugs already on the market upon the premise of a "benefit-risk" ratio, namely that the benefits are so tremendous that any "risk" is a minor consideration to be assumed by the cancer sufferer.

However, in actuality, the various cancer drugs approved previously by FDA are not beneficial and "curative", but are dangerous, even lethal and fatal, and many of them cause cancer, although designated as "anti-cancer" drugs.

Among these FDA-approved drugs are *Cytosan*, which according to FDA-approved manufacturer's labeling can cause death, also can cause cancer, and numerous other body-destroying effects. Likewise, *Adriamycin* can cause congestive heart failure, bone marrow depression, hemorrhage and numerous other ghastly effects. *Adrucil*, *BICNU*, *CeeNU*, *DTIC*, *Mutamycin*, *Matulane*, *Mithracin*, *FUDR*, *Fluorouracil*, *Methotrexate*, and *Blenoxane* are other drugs FDA-approved for "safety", and are severely toxic, and/or death-causing, cancer-causing, and all of them replete with a host of other undesirable and dangerous side effects.

Not one of these drugs is represented to be "curative."

### **Laws of the States To Be Ignored?**

Petitioner's brief contains not one word as to the laws of 19 states thus far enacted and approved for use of Laetrile.

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<sup>1</sup> For further information on the foregoing FDA-approved drugs, see "Physicians' Desk Reference", 1979, a standard reference work for doctors, monitored by FDA as to its contents.

The nineteen States are: Alaska; Arizona; Delaware; Florida; Idaho; Illinois; Indiana; Kansas; Louisiana; Maryland; Nevada; New Hampshire; New Jersey; North Dakota; Oklahoma; Oregon; South Dakota; Texas; and Washington.<sup>2</sup>

The Laetrile legislation in South Dakota was approved only as of March, 1979, and additional Laetrile legislation is pending in various other States.

The petitioner agency would have the Court believe that anyone who would employ Laetrile in any capacity is perpetrating a "fraud". Are we then to believe that the legislatures of 19 states are assisting in such "fraud", or is it more reasonable to believe that, for the first time in history, a drug has proved of such value for cancer sufferers that 19 states have deemed it appropriate and necessary to note by legislation its importance, a circumstance, which, the Society believes, has never occurred in the history of the United States?

### Any Compelling State Interest?

FDA argues herein that there is a "compelling state interest" which must be invoked by the Court to bar

<sup>2</sup> *Alaska* (See Alaska Statutes 08.64.367); *Arizona* (See A.R.S. 36-2451); *Delaware* (See Del. Code Ann. 16 Section 4901); *Florida* (See F.S.A. 458.24); *Idaho* (See Idaho Code 18-7301A); *Illinois* (See S.H.A. 56½, Section 1801); *Indiana* (See Burns Ind. St. Ann. 16-8-8-1); *Kansas* (See S.B. 505 May 8, 1978); *Louisiana* (See L.S.A.—R.S. 40:676); *Maryland* (See Ann. Code of MD, Art. 43 Sec. 133 ch. 809); *Nevada* (See Nev. Rev. St. 630.303); *New Hampshire* (See R.S.A. 329:30); *New Jersey* (See N.J.S.A. 24:6F-1); *North Dakota* (See H.B. 1214 eff. July 1, 1979); *Oklahoma* (See 63 Okl. St. Ann. Sec. 2-313); *Oregon* (See Oregon Rev. St. 689.885); *South Dakota* (Bill Number 1287 signed 3/16/79 eff. 7-1-79); *Texas* (See Vernon's Ann. Civ. St. 71 art. 4476-5a.); *Washington* (See R.C.W.A. 70.54.130).

Laetrile to everyone. The Society urges that this is simply not so.

John Stuart Mill, in his classic work, *On Liberty*, gives substance to the concept of "compelling state interest" when he asserts: "... one very simple principle, as entitled to govern absolutely the dealings of society with the individual in the way of compulsion and control, whether the means used be physical force in the form of legal penalties, or the moral coercion of public opinion. *That principle is, that the sole end for which mankind are warranted, individually or collectively, in interfering with the liberty of action of any of their number, is self-protection. That the only purpose for which power can be rightfully exercised over any member of a civilized community, against his will, is to prevent harm to others.* His own good, either physical or moral, is not a sufficient warrant. He cannot rightfully be compelled to do or forbear because it will be better for him to do so, because it will make him happier, because, in the opinions of others, to do so would be wise, or even right. These are good reasons for remonstrating with him, or reasoning with him, or persuading him, or entreating him, but not for compelling him, or visiting him with any evil in case he do otherwise. To justify that, the conduct from which it is desired to deter him, must be calculated to produce evil to some one else. The only part of the conduct of any one, for which he is amenable to society, is that which concerns others. In the part which merely concerns himself, his independence is, of right, absolute. Over himself, over his own body and mind, the individual is sovereign."

### Important Constitutional Rights Involved

The Constitutional right of privacy in the case at bar, as affecting both physician and patient, has been discerned and validated by this Court<sup>3</sup> in the parameters of the Bill



of Rights, and specifically within the language of the First, Fourth, Fifth, Ninth and Fourteenth Amendments to the Constitution. *Roe v. Wade*, 410 U.S. 113 (1973). This right has been recognized as a fundamental right guaranteed to the individual. *Griswold v. Connecticut*, 381 U.S. 479 (1965). One noted authority has described the central theme of the right of privacy as the individual freedom to make knowing choices as long as they do not adversely affect others. Beardsley, *Privacy: Autonomy and Selective Disclosure*, in *Privacy, Nomos XIII*, at 56 (1971).

The aspect of the right of privacy relating to personal autonomy is derived from the common law interest defined as the "right to be let alone." In his oft-quoted dissent, Justice Brandeis in *Olmstead v. United States*, 277 U.S. 438, 478 (1928), overruled in *Katz v. United States*, 389 U.S. 347, 352-53 (1967), stated:

"The makers of our Constitution undertook to secure conditions favorable to the pursuit of happiness. They recognized the significance of man's spiritual nature, of his feelings and of his intellect. They knew that only a part of the pain, pleasure and satisfactions of life are to be found in material things. They sought to protect Americans in their beliefs, their thoughts, their emotions and their sensations. They conferred, as against the government, the right to be let alone—the most comprehensive of rights and the right most valued by civilized men. To protect that right, every unjustifiable intrusion by the government upon the privacy of the individual, whatever the means employed, must be deemed a violation . . ."

This Court's modern privacy rulings have been strongly solicitous of individual choice in highly personal circumstances. See, e.g., *Griswold v. Connecticut*, *supra*, (1965); *Loving v. Virginia*, 388 U.S. 1 (1967); *Eisenstadt v. Baird*, 405 U.S. 438 (1972); *Roe v. Wade*, 410 U.S. 113 (1973);

*Doe v. Bolton*, 410 U.S. 179 (1973). Respondents are before this Court in the context of a similar highly personal situation. A denial of the right to choose Laetrile in the treatment of their *incurable disease* is, in what is a clear absence of a compelling interest on the part of petitioners, an unconstitutional denial of their fundamental right of privacy.

This Court established the right of a patient to choose an unapproved method of treatment in *Roe v. Wade* and *Doe v. Bolton*, *supra*. By acknowledging the right to undergo an unauthorized medical procedure, these cases went beyond the mere recognition of the patient's right to decline treatment or to choose a particular unapproved method of treatment.

Respondents' right to refuse medical treatment is incontrovertible. Should they decide to forego conventional treatments, as Glen Rutherford chose to forego a colostomy, do they not possess a further right to enlist such non-toxic treatments, however unconventional or distasteful to FDA they must be, as they may find to be of comfort? How can the informed cancer-ridden patient, who faces virtually certain death, be limited in choice of treatment administered by a state licensed physician to only Federally sanctioned alternatives?

## CONCLUSION

Man has gone through many stages in his search for health. He has tried many approaches. Many of these have proved to be blind alleys. He has learned bits and pieces. Some of what he has thought he has learned has proved not to be so. He once bled people and used leeches. He has since time immemorial experimented with herbs and foods. He has but recently begun to experiment with chemical drugs. In all of these attempts he has made what he

thought was progress. Sometimes there was real progress. Often, time showed that he has had to retract.

The Society does not claim that "orthodox" allopathic medicine has not made discoveries and has not experimented through the extensive use of drugs and surgery. But the Society does urge that conventional allopathic medicine and FDA have not yet cornered the market on truth.

The basic issues in this cause, despite any technicalities of statutes, or otherwise, reduce to a very simple circumstance:

1. When the State licenses a Doctor to treat the sick, by any and all means whatsoever, can he use his best judgment and discretion for the treatment and welfare of his patient, employing Laetrile or other therapies?

2. Or, does a bureaucratic instrumentality unaware of the needs of the patient or the condition of the patient dictate what the physician and patient shall do, superimposing State-dictated medicine?

Permitting one group to become a state-endowed monopoly is as dangerous in the healing arts as it is in economics or in political thought, perhaps more so, for here we are dealing with life itself.

Unfortunately man can be jealous of the known and reluctant to even consider what is new or different. History has shown that men of medicine and bureaucrats can be as narrow and uncompromising as other men. History has shown that many discoveries that we now consider significant were rejected by the "orthodox" and their discoveries hounded. History contains many examples to prove this point. Two late and distinguished Senators, Lister Hill of

Alabama and Paul Douglas of Illinois, had occasion to discuss this very matter on the floor of the United States Senate (109 Con. Rec. 14499):

Mr. Douglas. Is it not true that Joseph Lister was nearly driven out of the medical profession by the British Medical Association because he said that surgery which was not antiseptic gave rise to infections and caused great mortality among the patients?

Mr. Hill. He was subjected to many attacks.

Mr. Douglas. By the British Medical Association?

Mr. Hill. By men prominent in that association.

Mr. Douglas. Is it not true that Lister was merely following the teachings of the great French physiologist, Louis Pasteur, who discovered the germ theory of disease?

Mr. Hill. He applied the discoveries of Pasteur to surgery.

Mr. Douglas. Is it not true that Pasteur was nearly driven from his chair at the University of Paris by the doctors and physiologists of France?

Mr. Hill. That is correct.

Mr. Douglas. Looking back in history, is it not also true that Semmelweis—and in our country Oliver Wendell Holmes, Sr.—who discovered the cause of puerperal fever, resulting in death of women in childbirth—the cause being the dirty hands of doctors—was nearly driven from the profession?

Mr. Hill. The truth is that poor Semmelweis was a martyr to the cause. He died, driven and hounded to his death.

Mr. Douglas. He was driven to his death by the doctors?

Mr. Hill. That is true, because he insisted on washing his hands after he came out of the dissecting room, before he delivered a woman of a child.

Mr. Douglas. It was thought that that was a reflection on the medical profession, who believed that their hands were always clean and could not have anything on them that would infect others.

Mr. Hill. Yes.

Mr. Douglas. Is it not also true that Dr. Jenner, who developed the theory and practice of vaccination as a preventative, also was persecuted by the medical profession?

Mr. Hill. He was. He observed that the women in Scotland who milked cows and had cowpox largely secured an immunity from smallpox. That gave him the idea and he developed the vaccine which was the first vaccine we had against a dread disease.

Mr. Douglas. Is it not true that the teachings of Lister were brought to this country by the celebrated Dr. W. W. Keen, who, after the Civil War, went to Scotland and studied under Lister and then came back to practice in Philadelphia, and who was virtually driven out of practice in Philadelphia by the medical association and was only saved by some adventurous people on the board of the Pennsylvania General Hospital?

Mr. Hill. Dr. Keen was, according to history, the first American surgeon to use Lister's methods in Philadelphia.

Mr. Douglas. As a young man, I spent an evening with Dr. W. W. Keen, who spoke of the persecution he had been subjected to by the leaders of the medical profession in the city of Philadelphia.

Mr. Hill. He was a very remarkable man. Keen's 14-volume work was almost a bible for surgery procedures.

Mr. Douglas. Is it not true that Robert Koch, developer of 606, who did work on tuberculosis, suffered from persecution by the German medical association?

Mr. Hill. He did, as William Harvey, the discoverer of the circulation of the blood, had suffered.

Mr. Douglas. So the medical profession in many instances sought to persecute and defeat the professional men who were later hailed as great discoverers?

Mr. Hill. There are a great number of instances of that kind.

Nor is an almost interminable and prohibitively-expensive "new drug" proceeding with FDA an answer. For respondents, a class composed of terminally ill cancer patients, time is all. It has assumed, by definition but not by choice, an incalculable value.

"The final consequences (of petitioner FDA's ban on Laetrile) are ultimately borne by those whose bodies are the battleground on which cancer's war is waged." 438 F. Supp. 1287, 1300 (1977). Any legal right respondents possess to use Laetrile may be of academic value if secured only at some indetermined future time. For the terminally ill, the phrase "justice delayed is justice denied" contains special significance. Respondents ask simply that this Court remember that the acquisition of Laetrile for their own consumption is, *for them*, a matter of life and death and not one rightly governed by legal niceties. Respondents further ask that this Court reflect on the indescribable nature of the injury they must nevertheless attempt to describe, if they are to prevail here. This injury is clearly more than minimal or trivial; it is unconstitutional.

Respectfully submitted,

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78-605

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IN THE SUPREME COURT OF THE UNITED STATES

OCTOBER TERM, 1978

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UNITED STATES OF AMERICA, ET. AL., PETITIONERS

v.

GLENN L. RUTHERFORD, ET.AL.

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AMICUS CURIAE BRIEF BY THE NORTHWEST  
ACADEMY OF PREVENTIVE MEDICINE IN  
SUPPORT OF GLENN L. RUTHERFORD, ET AL.

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MOTION FOR LEAVE OF LATE FILING OF AMICUS  
CURIAE BRIEF

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IN THE SUPREME COURT OF THE UNITED STATES  
OCTOBER TERM, 1978

UNITED STATES OF AMERICA,  
ET AL.,

Petitioner,

v.

GLENN L. RUTHERFORD,  
Respondent.

NO. 78-605

MOTION FOR LEAVE  
OF LATE FILING  
OF AMICUS CURIAE  
BRIEF

COMES NOW GEORGE WM. CODY, counsel  
for the NORTHWEST ACADEMY OF PREVENTIVE  
MEDICINE, with regard to their interests  
Amicus Curiae, and moves this Court for  
Leave of Late Filing of Amicus Curiae  
Brief, filing date being on or before the  
6th day of April, 1979.

This Motion is based upon the records  
and files herein and upon the following  
affidavit of GEORGE WM. CODY.

CODY, HATCH, & BEDLE, INC., P.S.

151  
GEORGE WM. CODY, General Counsel  
DANIEL SMITH, Counsel and  
Member of the Supreme Court  
Bar

STATE OF WASHINGTON)  
COUNTY OF SNOHOMISH) ss

GEORGE WM. CODY; being first duly sworn  
upon oath deposes and says:

I am one of the counsel for the Northwest  
Academy of Preventive Medicine.

The interests of the Northwest Academy are  
such that their Amicus Curiae brief will  
present a viewpoint of value to the Court  
in determining this case. This case is very  
important to the interests of many physicians  
and their patients and is of first impression  
in this Court.

The Government's Brief with regard to the  
case, UNITED STATES OF AMERICA, ET.AL., v.  
RUTHERFORD, did not arrive in our office until  
the 26th day of March, 1979. The preparation  
of the Government's Brief was relief upon  
for the preparation of the Amicus Curiae  
Brief with respect to the Northwest Academy  
of Preventive Medicine. That two weeks time  
for preparation and printing of a brief is  
insufficient to prepare a proper document

for filing, and delivery to a printer for  
required printing.

/s/

GEORGE WM. CODY

SUBSCRIBED AND SWORN TO before me this \_\_\_\_  
day of \_\_\_\_\_, 1979.

Notary Public in and for  
the State of Washington  
residing at \_\_\_\_\_

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OCTOBER TERM, 1978

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No. 78-605

UNITED STATES OF AMERICAN, ET AL., Petitioners.

v.

GLENN L. RUTHERFORD, ET AL.

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AMICUS CURIAE BRIEF BY THE NORTHWEST  
ACADEMY OF PREVENTIVE MEDICINE  
IN SUPPORT OF  
GLENN L. RUTHERFORD, ET AL.

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INTERESTS OF THE PARTY AMICUS CURIAE

The Northwest Academy of Preventive Medicine is an association of doctors from various healing arts, including physicians and surgeons, osteopaths and surgeons, dentists, chiropractors, naturopathic physicians and members of other associated healing arts.

The purpose of the Academy is to further preventive medicine by: (1) organizing members who actively practice preventive medicine, (2) participating in the process

of education of the members of this association in various medical developments and techniques within the discipline; and (3) speaking out in areas of law and politics which effect the practice of preventive medicine.

Preventive medicine is a practice or concept of medicine designed to lead to the prevention of diseases and physical infirmities, rather than dealing with them solely after they have manifested themselves in some physical fashion. It has principally emerged within the last ten years as a distinct branch of medicine. Orthodox medicine, as represented by the American Medical Association and the American Cancer Society rejects one of the basic premises of preventive medicine. Preventive medicine relies upon clinical results to show the success of preventive medicine techniques. Clinical results are rejected as being "testimonials" or "anecdotal." This is easily ascertained by the agency's review of the testimony presented by proponents of Laetrile during the hearings conducted by the agency.

Preventive medicine thus differs from

"orthodox" medicine. Orthodox medicine is crisis and disease oriented. It is based upon the treatment of diseases and physical infirmities once they have clearly manifested themselves. Preventive medicine is designed to lead to the maintenance of health and the prevention of foreseeable infirmities. Thus rather than isolate and treat a specific cause of disease, preventive medicine takes the approach of supporting the body to maintain its own natural health rather than attacking disease with chemicals.

The Academy appears in this case to oppose the further entrenchment of the right of the Federal Food and Drug Administration (FDA) to limit the individual physician in his practice of medicine. This is accomplished by the FDA's limiting those medicinal substances which the physician may have available to utilize in his practice.

The Academy as an organization has not taken any stand with regard to the dispensation of Laetrile to the terminal ill cancer patient. Individual Academy members do, however, dispense Laetrile in the

course of their practice.

Proponents believe Laetrile is a body-supportive substance. It appears in its restorative propensities to assist the body to deal with cancer, rather than chemically attacking cancerous cells. This is within the Academy's conception of the proper practice of medicine.

Dispensing Laetrile is not a violation of law in states such as Washington. Eighteen states have now, by State law, authorized dispensing of Laetrile by qualified physicians. Two other states have had at least one-half of their legislatures pass bills which would allow such practice. It is apparent that there is a growing state trend to allow the dispensation of this medicinal substance within the sound discretion of the medical practitioner. The Federal Food and Drug Administration, through actions such as those reviewed by the lower court in this case, have endeavored to place severe limitations upon that practice.

The Academy has appeared as Amicus Curiae in the case of People v. Privitera, Jr.

\_\_\_\_ Cal 3d \_\_\_\_ (Sup. Ct. No. CR-32978



1979), recently decided by the California Supreme Court. The Academy was interested in Privitera because that case focused on issues concerning the State's right to intrude upon or regulate the relationship between a physician and patient.

An essential ingredient in any medical practice is the free exercise of the physician's treatment according to his own conscience based upon the medical needs and choice of the patient. Governmental interference should be minimized.

#### ADOPTION OF REFERENCE POINTS FROM THE BRIEF OF THE UNITED STATES

In this brief, the Academy would adopt by reference the sections of the Government's Brief entitled "Opinions Below", "Jurisdiction", "Questions Presented" and "Statutes Involved". The Academy would supplement the "Statement" section offered by the Government.

The case at bar first arose through the issuance of an injunction pursuant to the decision of the District Court of the Western District of Oklahoma, Luther L. Bohannon, Judge, 399 F. Supp 1208.

Judge Bohannon enjoined the Department of Health Education and Welfare (HEW) and the Food and Drug Administration from interference with a cancer patients' use of Laetrile. This injunction was issued pursuant to several findings which at this time are not pertinent to the case. On review, the Tenth Circuit Court of Appeals, at 542 F.2d 1137 (1976), affirmed the issuance of the injunction and remanded the case to the District Court to direct the Food and Drug Administration to prepare a full administrative record regarding the status of Laetrile in order that the entire matter could be reviewed by the Court.

The District Court, upon reviewing the findings of the Commission disagreed with the agency's analysis of the administrative record and found that the Commissioner's Ruling was arbitrary and capricious. Judge Bohannon again issued a sweeping injunction prohibiting the government from interference with the distribution and transportation of Laetrile.

The case was again reviewed by the Tenth Circuit Court of Appeals. It should be noted that this review was undertaken by three Judges other than those who heard

the original case. This time the Court of Appeals, in a very brief opinion, limited the trial court's second injunction and ordered the agency to

permit procurement of Laetrile for intravenous injections administered by a licensed medical practitioner to persons who are certified by a licensed medical practitioner to be terminally ill in some form.

# I.

## THE PHYSICIAN-PATIENT RELATIONSHIP SHOULD BE UNDISTURBED UNLESS GOVERNMENTAL INTERFERENCE IS REASONABLE AND NECESSARY

There is a Constitutional right of a physician to contribute his professional judgment to the physician/patient relationship free from unnecessary and unreasonable intrusion by the Government. There also is the Constitutional right of a patient to exercise his private medical perogatives free from this interference.

Some balance must be maintained between the rights that vest with the citizens and those interests of the Government which are just and reasonable. The tenor of the Tenth Circuit Court of Appeals opinion and of the District Court's review of the

administrative record was to the effect that these balancing determinations should be made whenever possible based upon a full administrative record which can be reviewed by the Courts. The primary cases in the area of the physicaains' and patients' rights are those noted briefly in the Government's Brief Roe v. Wade, 410 U.S. 113 (1973), and Doe v. Bolton, 410 U.S. 179 (1973). Particularly this is true of Doe v. Bolton.

In Doe v. Bolton, a Georgia Statute was under consideration which called for the initial decision of patient and physician regarding an abortion to be reviewed by Hospital Committees of other physicians. The mechanism being reviewed (which was stricken by the Court as violating Constitutional guidelines) concerned, therefore, the review of the treating physician's clinical judgment. In the circumstance at hand, the FDA has not compiled a record upon which it should seek to substitute the Commissioner's balancing of competing medical judgments for the individual physician's medical judgment.

In fact, the agency applies a different

standard to new drug applications not processed by pharmaceutical companies.

The Courts below seemed significantly aware of this. Considering a cancer victim's often rapid retrogression from apparent health to a terminal point, it cannot be doubted that any complex review mechanism that unnecessarily puts a grave strain on operational clinical judgment of an individual physician must be undertaken only if absolutely necessary. The Court noted in Doe v. Bolton, supra (at 197) with regard to the clinical judgment of a physician:

"Saying all this however does not settle the issue of the Constitutional propriety of the Committee requirement. Viewing the Georgia statute as a whole, we see no constitutionally justifiable pertinence in the structure for the advance approval by the abortion committee. With regard to the protection of potential life, the medical judgment is already completed prior to the committee stage, and review by a committee once removed from the diagnosis is basically redundant. We are not cited to any other surgical procedure made subject to committee approval as a matter of state criminal law. The woman's right to receive medical care in

accordance with her licensed physician's best judgment and the physician's right to administer it are substantially limited by this statutorily imposed overview . . . We conclude that the interposition of the hospital abortion committee is unduly restrictive of the patient's rights and needs that, at this point, are substantiated by her personal physician. To ask more serves neither the hospital nor the State." (410 U.S. 197-198)

The Georgia Statute required independent examination of the patient by two other licensed physicians. Concerning the relationship of the physician and patient in our society, the Court noted as follows:

The Statute's emphasis, as has been repetitively noted, is on the attending physician's 'best clinical judgment that an abortion is necessary.'

That should be sufficient. The reasons for the presence of the conformation step in the statute are perhaps apparent, but they are insufficient to withstand constitutional challenge. Again, no other voluntary medical or surgical procedure for which Georgia requires confirmation by two other physicians has been cited to us. If a physician is licensed by the State, he



is recognized by the State as capable of exercising acceptable clinical judgment. If he fails in this, professional censure and deprivation of his license are available remedies. Required acquiescence by co-practitioners has no rational connection with a patient's needs and unduly infringes on a physicians' right to practice. The attending physician will know when a consultation is advisable--the doubtful situation, the need for assurance when the medical decision is a delicate one, and the like. Physicians have followed this routine historically and know its usefulness and benefit for all concerned. It is still true today that '(r)eliance must be placed upon the assurance given by his license, issued by an authority competent to judge in that respect that he (the physician) possess the requisite qualifications,' (Dent v. West Virginia, 129 U.S. 114, 122-23 (1889)). See United States v. Vuitch, 402 U.S., at 71 (Doe v. Bolton, 410 U.S., 199, 200).

Finally, Justice Douglas in his concurring opinion was more cogent in his direct observation of these circumstances (at 219):

Physicians, who speak to us in Doe through an amicus brief, complain of the Georgia Act's interference with their practice of their profession.

The right of privacy has no more conspicuous place than in the physician-patient relationship, unless it be in the priest-penitent relationship.

It is one thing for a patient to agree that his physician may consult with another physician about her case. It is quite a different matter for the State compulsorily to impose on that physician-patient relationship another layer of physicians. The right of privacy--the right to care for one's health and person and to seek out a physician of one's own choice protected by the Fourteenth Amendment--becomes a matter of theory, not a reality, when a multiple-physician-approval system is mandated by the State. The State licenses a physician. If he is derelict or faithless, the procedures available to punish him or to deprive him of his license are well known. He is entitled to procedural due process before professional disciplinary sanctions may be imposed. See In re Ruffalo, 390 U.S. 544. Crucial here, however is state-imposed control over the medical decision whether pregnancy should be interrupted. The good-faith decision of the patient's chosen physician is overridden and the final decision passed onto others in whose selection the patient has no part. This is a total destruction of the

right of privacy between physician and patient and the intimacy of relation which that entails.

It should further be noted that Whalen v. Roe, 97 S.Ct. 869 (1977) did nothing to eliminate the physician's right nor denigrate that right other than to note that it was no stronger than that of the patient to whom it attaches. The Court, while not having directly addressed the entire issue, has begun to touch the area of the right of the physician to exercise his best medical judgment and the right of the patient to rely thereon. In examining the administrative record, it is urged by this Amicus Appearance that the Court bear in mind that a significant number of medical minds indicated their satisfaction with the relative safety and effectiveness of Laetrile, and the Court if at all possible should recognize the Constitutional rights of the physician and patient in order to leave this determination undisturbed. This Court should not allow the agency to substitute its judgment for the physician's judgment when evidence has been presented by Laetrile proponents of equal or greater value to the evidence in opposition to

Laetrile.

A medical doctor is, under general rule of evidence, deemed to be an expert in medical areas. This results from his educational background, experience and licensing. There is a direct reason for this. As long ago as Dent v. West Virginia, 129 U.S. 1114, 95 S.Ct. 231 (1889), the Court established the following proposition (at 1122,23):

Few professions require more careful preparation by one who seeks to enter it than that of medicine. It has to deal with all those subtle and mysterious influences upon which life and health depend and requires not only a knowledge of the properties of vegetable and mineral substances, but of the human body in all its complicated parts and their relation to each other, as well as their influence upon the mind. . . . Everyone may have occasion to consult (a physician), but comparatively few can judge the qualifications of learning and skill which he possesses. Reliance must be placed upon assurance given by his license. . . . that he possesses the requisite qualifications.

Further, various Courts have cited with approval U.S. v. Freund, 290 F.411 (D.C. Mont. 1922). This case considered the

constitutionality of a prohibition era statute which restricted the amount of alcohol a physician could prescribe. The Court noted:

It is an extravagant and unreasonable attempt to subordinate the judgment of the attending physician to that of Congress, with respect to matters with which the former alone is competent to deal and infringes upon the duty of a physician to prescribe in accordance with his honest judgment and upon the right of the patient to receive the benefit of the judgment of the physician of his choice. (emphasis added)

Without even discussing the doctrine of privacy, as originally formulated in the Olmstead dissenting opinion by Justice Brandeis, it can be seen that, in general, the medical judgment of a physician with proper training and proper scientific evidence and background has in many instances remained undisturbed by the Court. It is urged in this Amicus Appearance that the Court consider the fact that the delicate balance between the physician and patient is irreparably disturbed by allowing the agency to simply balance one group of

medical witnesses against another.

The Supreme Court of the State of California has recently addressed the issue of regulating Laetrile. People v. Privitera, et al., \_\_\_\_ Cal 3d \_\_\_\_ (1979) overruling People of the State of California v. Privitera, et al., 141 Cal. Rpt. 764 (1977). That as yet unreported decision of that Court was a five to two decision, with the two dissenters adopting the lower court decision.

The California Supreme Court majority simply held that the California Statute represented a reasonable intrusion by the State on the rights of both patients and physicians. That decision, however, dealt directly with the constitutionality of the California statute. The California Supreme Court differentiated that application of state power from Judge Bohannon's Rutherford decision. The Court noted that this Rutherford decision dealt with a class action by terminally ill cancer patients; the case before them dealt with criminal violation which was conspiracy to violate the laws of the State of California through the dispensation of an unrecognized cancer remedy. There is a specific California



Statute regulating the development of cancer treatments.

This does not, however, completely obviate the vitality of certain of the lower court rulings which recognized the constitutional arguments dealt with in this brief and accepted by Judge Bohannon.

This Court is urged to accept the reasoning of the Privitera court of appeals. The discussion at 141 Cal Rptr. 764, 770, will be briefly recreated here verbatim as it is exceptionally pertinent to these issues. The Court for other issues relied heavily upon the language of Rutherford v. United States, 438 F.Supp 1287(1978)(the California Supreme Court did not challenge the validity of this case doctrine established by Rutherford but differentiated it):

Dr. Privitera asserts a separate and distinct constitutionally protected right--a zone of privacy--to prescribe, to treat patients whether in the orthodox mode--free from unjustified state interference.

Whalen v. Roe, supra, \_\_\_ U.S. \_\_\_ (97 S.Ct. 869) accepts as a premise the existence of the right of the individual patient to choose independently with the advice of his physician to use or not to use

a particular medication. Said the Supreme Court at page 878:

"Nor can it be said that any individual has been deprived of the right to decide independently, with the advice of his physician, to acquire and to use needed medication."

However, with respect to the doctor's right to freedom to treat, to minister to the sick, in Whalen v. Roe, supra, \_\_\_ U.S. \_\_\_ (97 S.Ct. 869), we have heretofore noted the Supreme Court's determination the "doctor's claim is derivative from, and therefore no stronger than, the patients'." Doe v. Bolton, supra, 410 U.S. 179 (97 S.Ct. 739), however, speaks specifically of the doctor's right to administer medical care. Bolton involved a constitutionally defective statute requiring consent of two state licensed physicians other than the patient's own doctor before an abortion could be performed as well as advance approval of three members of the hospital staff where the abortion was to be performed. Concerning this statute the Supreme Court said:

"The woman's right to receive medical care in accordance with her licensed physician's best judgment and the physician's right to administer it are substantially limited by this statutorily imposed overview." Doe v. Bolton, supra, 410 U.S.

179, 197 (93 S.Ct. 739, 750);  
emphasis added.)

Dr. Privitera additionally asserts an independent right to treat, not derived from or measured by his patient's right of choice, without first obtaining approval of the procedure or drug prescribed from a governmental board. He argues Health and Safety Code section 1707.1 invades this right. Again, as in the right of the patient, the doctor's asserted right must be first examined to determine its nature and thereby select the test, the degree of scrutiny to which the state interference will be put. The right found must be balanced against the state--the public interest protected.

Dr. Privitera's right, in relation to the patient, has been viewed traditionally as a species of economic interest rather than as "fundamental" akin to the privacy right. If a rational basis was found to support an encroachment, the statute was sustained.

While a dispassionate reading of the physician's licensing requirements raises some question concerning the total rationality of the licensing scheme, such standards are generally upheld as reasonable and necessary means of protecting the public health.

The more recent cases hint at the more profound right in the doctor. It is postulated: There exists in the doctor licensed to practice medicine a right, constitutional in nature, as

yet ill-defined, to treat and to treat by unorthodox modalities --as yet unapproved by the state board--an informed consenting patient.

Doe v. Bolton, supra, 410 U.S. 179, 201 (93 S.Ct. 739, 751), states if a physician is licensed by the state he is recognized by the state as capable of expressing acceptable clinical judgment. If he fails in this, professional censure and deprivation of his license are remedies available and "reliance must be placed on the assurance given by his license. . . that he possesses the requisite qualifications."

Roe v. Wade, supra, 410 U.S. 113, 163 (93 S.Ct. 705, 732), states concerning the termination of pregnancy during the first trimester:

" . . . the attending physician, in consultation with his patient, is free to determine, without regulation by the State, that, in his medical judgment, the patient's pregnancy should be terminated." (Emphasis added)

Reason, based on history, experience, supports the doctor's premise. To require prior state approval before advising--prescribing-administering--a new treatment modality for an informed consenting patient is to suppress innovation by the person best qualified to make medical progress. The treating doctor, the clinician, is at the cutting edge of medical knowledge. To require the doctor to use only orthodox

"state sanctioned" methods of treatment under threat of criminal penalty for variance is to invite a repetition in California of the Soviet experience with "Lysenkoism." The mention of a requirement that licensed doctors must prescribe treat within "state sanctioned alternatives" raises the spector of medical stagnation at best, statism, paternalistic Big Brother at worst. It is by the alternatives to orthodoxy that medical progress has been made. A free, progressive society has an enormous stake in recognizing and protecting this right of the physician.

## II.

### THE CASE AT BAR CAN BE DISTINGUISHED FROM OTHER DETERMINATION OF FDA AUTHORITY AND OTHER LAETRILE CASES

The Government's Brief dealt with the case law standards set since the enactment of the 1962 Amendments to the Food and Drug Act requiring new drug applications (21 U.S.C. Section 355). These standards are delineated in U.S. v. Article of Drug "Bentex Ulcerine", 469 F.2d 875 (1972) and U.S. v. Articles of Drug "Colchicine", 442 F.Supp 1236 (19 ).

Prior to the case at bar the finding that a drug is a "new drug" as defined by 21 U.S.C. Section 321 (p) required an applica-

tion initially established by that agency. Once this was established, any exemptions sought under the "grandfather clause" were required to be established in each of the necessary element by the proponent. (The five elements cited in the Government's Brief are those established by previous case law.)

The Courts in the two above-cited cases held that a desirable record for such exemption should show a wide-spread usage of the drug in question, pursuant to adequate testing by recognized experts in a given medical area sufficient to establish the efficacy of that substance. This administrative showing should include the fact that the usages, labeling, and recommended dosages were the same as those factors prior to the triggering date of the 1962 Act as after that date. The Courts have further held that any change in one of these factors, or any additional claim for efficacy attributed to the drug after the triggering date, would require a new drug application with regard to these developments. It has been argued by the Government in previous cases that any



of these changes, even as slight as a labeling change, should require, as a matter of law a complete new drug application for the entire product as if it were not a pre-1962 drug.

Both of the cases cited above involved products which were distributed throughout a limited geographical area. Bentex Ulcerine was a localized medicinal product recommended for treatment of peptic ulcers. Colchicine was similarly limited to a geographical area as a treatment for Gran Mal seizures. There had been a slight labeling change over a period of years, and due to the small geographical area over which the products were distributed, the recognition by medical doctors for safety in use was limited to a relatively small geographical area.

Both Courts found it appropriate to prohibit transportation of that substance in interstate commerce as the FDA had sought. The FDA would have this authority until appropriate new drug applications had been completely processed and favorably passed upon by the agency. These Court holdings were based on a finding

that the safety of the substance was not sufficiently established within the terms of the grandfather clause.

Durovic v. Richardson, 479 F.2d 242 (7th Cir) (1973) dealt with the proposed cancer remedy Krebiozen. The Court here made a basic finding that even prior to the triggering date of October 10, 1962, in the case of a drug to be used as a treatment for a life-threatening disease, the term "safety" had incorporated the concept of effectiveness. The Court found that the proponents of Krebiozen had failed to establish by a preponderance of the evidence that the drug was both safe and effective within this construction of the Act.

This is the argument which is urged to this Court by the Government's Brief. This construction of statutory language was rejected by the Tenth Circuit Court of Appeal in its review of the case at bar. In its first decision in this case, the Court found implicitly that the addition of "effectiveness" requirement was a new one with the Acts' 1962 amendments. As the Court noted:

Prior to the 1962 Amendment, the only prerequisite for a drug to avoid classification as a new drug was recognition that it was safe. But the 1962 Amendment added the requirement of "effectiveness" (citing statute). Rutherford v. United States, 542 F.2d 1137, 1141 (1976)

The Court placed the burden on remand with the agency for the creation of a record to show affirmatively and substantially by the evidence, that Laetrile was not only a new drug within the terms of the statutory enactment, but also that it was subject to a new drug application because it did not fall within any appropriate exemptions.

The Court noted in this regard at 1143:

The FDA has argued that they have not issued any regulation or rule which specifically or positively forbids the administration of Laetrile. This is true. However, the FDA has made an administrative determination that Laetrile is a new drug and this places the Plaintiff in a position in which he has to admit that it is a new drug in order to get the FDA to move. As a result he could not be heard to say that they have effectively stymied the use of this drug. The FDA has done this without citing any facts whatsoever, merely a conclusion, and this is the kind of declaratory order that was before

the Court in Weinberger v. Hynson, Wescott & Dunning, Inc., 412 U.S. 609, 625-27, 93 S.Ct. 2469, 37 L.Ed.2d 207 (1973)

In its analysis of the relationship between safety and efficacy requirements, and in its act of placing the burden upon the agency to establish, by a proper record, that the agency has authority over the distribution and transportation of Laetrile the Tenth Circuit has differed in its approach from the previous decisions. It is the balancing of these two approaches which this Court must undertake in rendering its opinion. Through this Amicus Appearance the Northwest Academy would urge the court to follow the approach of the Tenth Circuit Court of Appeals.

Laetrile has given rise to other judicial discussion of these issues. In these cases the Court has placed the burden upon the proponents of Laetrile to establish that the drug should be exempted from Federal Regulation. This line has been followed with the exception in Rizzo v. U.S., 432 F.Supp. 356 (1977) which followed the authority of the earlier Rutherford case.

In some of these cases this approach has

been appropriate. Cases have been brought by individual cancer patients seeking preliminary injunctions. Quite rightfully, these Courts have placed a high burden on the patient to establish at the preliminary injunction stage that there is a sound chance of the patient prevailing at trial. Unfortunately, in each of these cases where injunctions were denied, the patient was deceased long before the matter came to trial.

The first such case is Gadler v. U.S., 425 F.Supp. 244 (1977). Petitioner Gadler filed a Motion for Preliminary Injunction seeking to restrain government defendants from barring his personal importation of Laetrile from Mexico. The Court denied the requested injunction. The Court found that the substance was a "drug" within the meaning of the Act. The Court examined the various claims of the Petitioner for exemption, noting at the outset that a substantial burden was placed upon the Petitioner to establish a probability of success on the various issues when the matter went to trial. The Court took a posture similar to that urged here by the Government, finding that

the Petitioner had not carried his claim that the substance was not a new drug, nor that the provisions of the Act which allowed prohibition of the drug's movement in interstate commerce did not apply to his personal use of the substance. The Court denied the request for injunctive relief.

The case of Rizzo v. U.S. supra, arose after the first Rutherford decision from the Tenth Circuit Court of Appeals. Citing Rutherford as its principal authority, the Court granted injunctive relief to the Petitioner Rizzo, limiting the Government's intervention of his importation and usage of Laetrile. The Court felt that the Petitioner raised serious statutory and constitutional issues which were fairly designed for appropriate litigation. The Court further recognized that in balancing the equities between the needs of the agency and the needs of Rizzo, a cancer patient seeking access to a medication that he had determined was a desirable treatment, must have tipped this balance in his favor. The Court found that the patient would indeed suffer irreparable injury if the injunction was denied. He could readily anticipate



imminent death.

The Rizzo court addressed some specific statutory issues and found that these conflicting issues were indeed difficult and complex and ultimately in need of a careful determination. The Court addressed its own two-fold Constitutional concerns. Firstly, this Court was concerned with the individual's right to self determination in medical areas as a facet of his right to privacy.<sup>1</sup> Secondly, the Court was concerned with the lack of due process in the agency's actions regarding Rizzo.

The Rizzo Court noted that the parameters of an individual's right to privacy in medical elections had not been completely defined. Prior Supreme

1. It should be noted here, as related by author Robert L. Schwartz in the February 1979 issue of the American Bar Association Journal, that Doctor Benjamin Rush as one of the country's founding fathers felt that the only way to adequately protect this type of right to privacy was to create a right to medical thought similar to the right of religious freedom. Such right would have attached both to the patient and to the physician. Although this concept was not adopted directly by the founding fathers, it is of historical significance that this was a matter of concern at least to some of the founding fathers.

Court cases had dealt with some of these issues. See, Roe v. Wade, supra, and Doe v. Bolton, supra. The Court's concern was that such parameters as existed can not be infringed upon by Government action. The Court was further concerned that the agency's action brooked Rizzo's right to be free from deprivation of life, liberty and property without due process of law. The Court expressed grave concern that an individual such as Rizzo was simply not in a position to fund the type of new drug application the agency was requiring. This jeopardized his ability to protect his self-determination as well as his life, liberty and property.

The Rizzo Court also addressed one other issue of concern to the Northwest Academy. Rizzo was suffering from cancer of the pancreas. The Court analyzed in a brief discussion the recommended and recognized treatments considered safe and effective by the agency. Specifically, the Court considered the prescription of Fluororacil, a highly toxic drug which the Court noted was described by the manufacturer's own package insert:

Fluororacil is a highly toxic drug with a narrow margin of safety. Therefore, patients should be carefully supervised since thereapeutic response is unlikely to occur without some evidence of toxicity. Patients should be informed of expected toxic effects, particularly oral manisfestations. White blood counts with differential are recommended before each dose. Severe hemotological toxicity, gastrointestinal hemorrhage and even death may result from the use of Fluoraracil despite meticulous selection of patients and careful adjustment of dosage.

These are the recent cases in which the Court's have considered the individual's right in these medical areas. Other cases as noted by the Government have considered Laetrile as a medical substance. All of these have been unfavorable to the drug's proponents. Most of these cases, however, involve small manufacturers or suppliers who were generating a substance and putting it into interstate commerce for sale. In this regard, the Federal District Courts have been particularly unreceptive to such parties.

### III.

#### THE FDA HAS THE BURDEN OF ESTABLISHING THAT IT HAS AUTHORITY TO REGULATE THE DISTRIBUTION OF LAETRILE

The Tenth Circuit has for the first time required the Agency to meet the burden of establishing affirmatively its regulatory authority vis a vis Laetrile. Opinions of the District Court and the Tenth Circuit Court of Appeals contained a great deal of that which is an application of common sense and reasonable logic, rather than an application of existing law. Prior to these decisions, there had been little court action favorable to opponents of the wide-spread and wide-ranging authority exercised by the Food and Drug Administration.

Much of the case law in this area is not directly supportive of the actions taken by these courts below. These Courts have moved in a new direction with regard to the authority of the FDA. Since those decisions have been announced, other Courts have followed this lead, and curtailed the FDA's authority. It is perhaps the case that some trial courts were simply awaiting some legal authority for this

type of action.

Laetrile is a pharmaceutical product or medicinal substance that strikes against the grain of establishment medical research and development. It is not exceptionally costly nor complicated to produce. It is not a substance which is limited in its production to large pharmaceutical companies. The interests of the pharmaceutical companies is frequently the same as those of orthodox medicine. The development of this substance, for philosophical reasons, goes against the principals of modern orthodox medicine.

The FDA requirements for the processing of a new drug application require an extreme expenditure of time, energy and money. These expenditures can normally only be underwritten by pharmaceutical houses which have significant profit possibilities from the production of their pharmaceutical products. This has not been undertaken with regard to the substance Laetrile. Medicine's interests are frequently the same as those of the pharmaceutical industry.

As presently administered by the FDA

in cases of a new drug application, there is the necessary expenditure of resources beyond the capacity of anyone outside the established pharmaceutical industry. Without this expenditure, the applications are deemed incomplete by the FDA.

The Tenth Circuit Court of Appeals seemed aware of this financial discrepancy. Previous cases, including those cited by the Government place the burden on the proponents of the pharmaceutical product, even where the proponent was a single individual, to establish the right to exemption status for the product in question under the "Grandfather Clause" of the 1962 Act.

In several of these previous cases that pharmaceutical product was Laetrile. However, these cases lacked an administrative record. The first time the case at bar appeared before the Tenth Circuit Court of Appeals, this was acknowledged by the Court. The Court stated:

From what has been said it is obvious that we are not in agreement with the trial court's opinion that the FDA has to approve or disapprove any new drug, even in the absence of



an application, that satisfies the statutory mandate. As we have noted, Section 505(b) of the Act specifically requires the filing of a new application by the proponent of a new drug. The FDA simply rules on the application as submitted.

(a) See H.R. Rep. No. 2139, 75th Cong. 3d Sess. (April 14, 1938) at 9:

This provision (Section 505) will not put the Federal Government into the business of developing new drugs, nor will it require the Government to duplicate laboratory and clinical tests made by responsible manufacturers. The provision merely sets up a method for the authoritative review of the manufacturer's tests and will not unreasonably delay the introduction of new drugs in the market. It provides for court review of the decision of the administrative agency adverse to the manufacturer.

(See also H.R. Rep. No. 2464 87th Cong., 2d Sess. (September 22, 1975) at 3.)

Congress in writing Section 505 (b) was relying on the ability and willingness of the pharmaceutical companies to present new drugs. It follows that the FDA was not compelled to pursue

this new drug procedure in the absence of an application. (Citations omitted)

We are unable, however, to see how the FDA can avail the obligation of producing an administrative record to support its determination of the first and more fundamental issue that Laetrile is a new drug, for it is not a new drug merely because they say it is. Moreover, such a conclusory ruling precludes effective review under 5 U.S.C. Section 706 (2). Cf Weinberger v. Hynson, Wescott & Dunning Inc., supra which holds the new drug decision by way of 5 U.S.C. Section 554(e) to be reviewable in a district court. To support its determination the FDA in the case at bar would have to present substantial evidence to support that proposition that Laetrile is not generally recognized among qualified experts as "safe and effective": and that Laetrile is not grandfathered by either of the exemptions discussed above.

It seems doubtful that the FDA has in fact developed an administrative record adequate under 5 U.S.C. Section 554(c) and hence there is probably nothing which is presently available for a court to review. Nothing in the record

suggests that the FDA has dealt with Laetrile in a rule making proceeding under Section 701 of the Act, 21 U.S.C. Section 371, Compare National Nutritional Foods Ass'n v. Weinberger, 512 F.2d 688 (2d Cir. 1975). Hence, if this is true the appropriate procedure for the district court is to remand the case back to the FDA for proceedings adequate to develop a record supportive of the agency's determination the proceedings should give Laetrile proponents an opportunity to express their views. This is a result which is also supported by the Supreme Court decision in Weinberger v. Bentex Pharmaceuticals, 412 U.S. 645, 93 S.Ct. 2788, 37 L.Ed.2d 235 (1973). There the district court faced with a similar problem referred the matter to the FDA for initial determination. See 412 U.S. at 652-54, 93 S.Ct. 2788. The question whether the drug is to be recognized as "safe and effective" or was "grandfathered in" are "the kinds of issues particularly suited to initial determination by the FDA." Id. at 653, 93 S.Ct. at 2494. Rutherford v. United States, 542 F.2d 1137 (1976) at pp. 1143-1144.

Balancing these equities, and considering the Constitutional right of privacy

that accrues to the physician-patient relationship, it is reasonable to require the FDA to clearly establish the basis for its regulation of Laetrile.

#### IV.

#### THE FDA FAILED TO MEET ITS BURDEN OF SHOWING IT HAS THE AUTHORITY TO REGULATE LAETRILE

The Tenth Circuit Court of Appeals decision which is before this Court is that Court's second consideration of the Laetrile issue. This opinion is very brief by normal standards. The Court did not pass on the merits of Judge Bohannon's review of the FDA's administrative record. The Court held that it could not uphold the agency's action when the consideration was the "safety" and "effectiveness" of a substance which is proposed to be provided to "terminally ill" cancer patients after orthodox treatments have failed to restore these patients' health. We would also urge that the Court consider the merits of Judge Bohannon's review of the administrative record.

In line with the first decision of the

Tenth Circuit Court of Appeals, Judge Bohannon has correctly balanced the various equities of the parties. He has taken cognizance, as was done in Rizzo v. U.S. supra, (which cited as its basic authority the first Rutherford case, 542 F.2d 1137 (1976)), that the size of the pharmaceutical companies and the nature of "orthodox medicine" has meant that no standard has been applied to other orthodox cancer treatments similar to the one the agency has applied to Laetrile. The medicinal substances used in Chemotherapy cannot rationally be described as "effective" or "safe". The representation by medical authorities has been that these substances, though exceptionally hazardous to any individual's health, are necessary treatments; in a relatively small percentage of cases some remission of cancer cells can be achieved without completely leading to the termination of the patient.

Judge Bohannon noted that there is no "majority" medical opinion with regard to balancing such factors in cancer treatment. In point of fact, only the proponents experts had utilized Laetrile;

the opponents criticized their "standards". But the bureaucratic weight of the agency and its authority has been thrown behind the orthodox medical acceptance of Chemotherapy and not behind Laetrile. Both Judge Bohannon and the Tenth Circuit would require that the Government show that each Government intervention into the distribution and transportation of a medical product be necessary and reasonable, not simply concurred in by "orthodox" medicine.

Judge Bohannon also considered the Constitutional issues concerned in this conflict between the FDA and individual rights. These issues have already been discussed above.

#### V.

#### THE FDA HAS NO AUTHORITY TO INTERFERE WITH THE USE OF LAETRILE BY THE TERMINALLY ILL

The Tenth Circuit Court of Appeals in the decision on appeal to this Court, omits discussion of several aspects of the District Court's decision. The Court deals simply and briefly with the concept that the action, having been



brought by a class of terminally ill patients, must concern the issues of safety and efficacy of Laetrile as a drug when dispensed to such a class.

This brief has previously urged that each individual substance must be examined with regard to reasonable application of the agency's standards. The Court has held that, regardless of the drug in question, the terms "safety" and "effectiveness" have no medical application to the terminally ill as a class.

It is true, that the Court does not define the terms "terminally ill". The Tenth Circuit noted in its opinion that the determination of this medical status can be made by any licensed medical doctor who is competent to practice. Therefore, the determination as to whom the standards created by the Court shall apply should be left to licensed medical practitioner.

The Court relied upon no apparent case law or legal authority in formulating these standards. It noted that it was within its authority in directing the agency to compile an appropriate record.

It was within the authority of the District Court to review the findings and the District Court had done so. Further, the Court noted (citing Weinberger v. Hynson, Wescott & Dunning Inc., supra) that the Courts possess the power to review the determinations made by the agency, basing its considerations on determination of "all relevant questions of law".

The Court notes, at page 6(a) of the Petitioner's appendix, that with regard to terminally ill cancer patients, Laetrile is "as effective as anything else". The Court notes (again at 6(a)):

We do not say that anything is safe for the persons concerned and nothing is effective, but it is apparent that no applicable or reasonable measure exists. (Emphasis provided)

The Government has argued that the real danger and lack of safety in a substance such as Laetrile is that unauthorized individuals may abuse the substance by obtaining it once it has been released into the market place. We would argue that this concept applies equally to all substances or products

regulated by the FDA. Any regulation is subject to abuse. If Laetrile is released some control will undoubtedly be placed over its usage within the guidelines established by the Court. The Court dealt with this issue in its opinion. The Court stated at pages 6(a) and 7(a) of the Government's appendix as follows:

We are well aware of and have considered the argument that some patients will be victimized by unscrupulous persons who will seek to profit by offering Laetrile as a "cure". This is however not a legal matter, but an administrative or regulatory problem of the FDA.

The Court thus directly placed the burden on the FDA to carry out the Court's decision and also appropriate legislative mandates. It is no objection to such authority of the Court that the agency disagrees with the directive it has been given.

The Tenth Circuit did not deal directly with the issues dealt with by the District Court. It did not indicate that it disapproves of them; it simply did not discuss them. The Court noted specifically

that it did not reach the Constitutional issues discussed by the District Court.

The decision of the Tenth Circuit Court of Appeals had its own wisdom and its own logic, which this Amicus Appearance urges this Court to accept. The reasoning applied shows directly and logically the fallacy in the agency's thinking. We would urge the Court to consider that the reasonableness of each request and each situation must be determined by the agency by applying reasonableness and logic to each circumstance. The agency should not be permitted to simply fall back upon its own determination that no new drug application has been processed. We would further urge that the Court consider the issues addressed by the District Court, especially with regard to the Constitutional aspects of the case.

## CONCLUSION

The Northwest Academy of Preventive Medicine urges the Supreme Court to affirm the decision and holding of the Tenth Circuit Court of Appeals and the reasoning of the District Court.

Respectfully submitted,

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